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EMERGENCY TREATMENT OF CARDIAC ARRHYTHMIAS

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and
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The cardiac arrhythmias often present themselves as grave emergencies. Fortunately, these disorders usually respond rapidly and dramatically to therapy. Simple, intelligent treatment of a serious arrhythmia, administered by the wise physician, frequently can be lifesaving. As a result of continuing research, the number of deaths resulting from arrhythmias can now be reduced much more radically than was formerly possible. This may be accomplished by proper use of four main therapeutic measures: (1) the rapidly acting digitalis preparations, (2) quinidine, (3) procaine amide (Pronestyl) hydrochloride, and (4) carotid sinus stimulation.

THERAPEUTIC DRUGS AND PROCEDURES

Of the purified digitalis preparations, lanatoside C (Cedilanid) is one of the most widely used in America.[1] This drug acts rapidly and is eliminated quickly. Intramuscular administration is generally preferred because of its greater margin of safety. In emergencies, however, lanatoside C may be given intravenously. The full digitalization dose is about 1.2 to 1.6 mg. or 6 to 8 cc.[1] but varies in different cases. Divided doses are usually given; for example, 1.2 mg. or 6 cc. is given initially, followed, if necessary, in one hour by 0.4 mg. or 2 cc.

A second digitalis preparation of value in emergencies is ouabain. This drug has been in general use abroad for many years and is now becoming widely employed in America. Since ouabain acts even more rapidly than lanatoside C it may be used when an immediate effect is urgently required. A dose of 0.5 mg. followed hourly by 0.1 mg. is given intravenously until the desired effect has been obtained or a total of 1 mg. has been administered.[2] Ouabain, ready for injection, is available in 0.5 cc. ampuls, containing 0.1 mg., and in 2 cc. ampuls, containing 0.5 mg. of the drug in aqueous solution. The solution is preferably diluted in 150 to 500 cc. of glucose and given slowly as a drip infusion over a period of 30 minutes to 3 hours, depending on the degree of emergency.[3]

Quinidine.—Although quinidine usually is given orally, it may be administered intramuscularly or intravenously. When used orally or intramuscularly, the initial course of quinidine consists of 0.2 gm. doses every two hours until the arrhythmia has been abolished or a total of 1 gm. has been given. If the arrhythmia continues, the dose may be increased to 0.4 gm. every two hours. A third course using doses of 0.6 gm. may be necessary. Rarely, even larger doses are required but are likely to give rise to toxic effects. Oral administration of quinidine on an around-the-clock schedule is made considerably less inconvenient by the use of delayed absorptive-coated tablets.[4] These tablets, taken at bedtime, provide adequate medication until the following morning and enable the patient to obtain an uninterrupted night of sleep. Quinidine lactate and gluconate are excellent preparations for parenteral use. The lactate is available in 10 cc. ampuls containing 0.65 gm. of quinidine. Intravenous injection previously was advisable only in emergencies but now can be carried out with relative safety by means of the following procedure: The lactate is diluted in 50 to 150 cc. of 5% glucose and introduced into the vein by the drip method at a rate of 2 cc. per minute. Electrocardiograms should be taken throughout the injection. As reported by Clagett[5] and confirmed by our experience, this method is considerably safer than intramuscular or more conventional intravenous injections because use of the drug may be discontinued when normal rhythm is restored or when toxic reactions appear. Digitalis and other drugs can be given with safety by the same method. Thus the intravenous route need no longer be considered more hazardous than slower intramuscular therapy.

Procaine Amide (Pronestyl).—The efficacy of procaine in the prevention and treatment of ventricular arrhythmias has been known for a number of years. Undesirable side-effects, however, severely limited the use of this agent in concentrations adequate to control ar-

From the Institute for Medical Research, Cedars of Lebanon Hospital, and the Department of Medicine, University of California School of Medicine.
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rhythmias.[6] With the introduction of procaine amide, these reactions have been largely abolished. Procaine amide originally was believed to be of therapeutic value only in ventricular arrhythmias,[7] but recent experience has established its usefulness in the management of auricular arrhythmias.[8] The drug may be given orally, intramuscularly,[9] or intravenously. The dose is usually 250 to 500 mg. repeated in two hours, but larger amounts sometimes are required. Since procaine amide is rapidly effective when given intramuscularly, the more hazardous intravenous route rarely need be used. Solutions containing 100 mg. of procaine amide per 100 cc. are available for parenteral injection. When the drug is given intravenously, the rate of injection should not exceed 100 mg. per minute.[10] Procaine amide is relatively harmless in most instances but has been known to give rise to serious ventricular arrhythmias,[11] agranulocytosis,[12] dermatoses,[13] and psychosis,[8g] as well as nausea and vomiting.[8d]

Carotid Sinus Stimulation.—Paroxysms of auricular tachycardia often can be terminated abruptly by massage of the carotid sinus. Unfortunately there is frequently pressure over the carotid sinus instead of the proper procedure of massage.[14] Many physicians have reported that carotid sinus stimulation proved ineffective, when actually their maneuver resulted only in obliteration of the carotid artery below the sinus. The patient should be recumbent with a pillow under his neck and his head turned to one side. After the carotid sinus is located as a bulge on the artery, the thumb is used to administer slow but firm strokes up and down the sinus. Massage should be done first on the right side, then on the left: both sides should never be stimulated simultaneously. The duration of the procedure is governed by instructing the patient to count aloud slowly to 20. This device distracts the patient from the annoying maneuver and also provides the physician with a maximum time limit for uninterrupted massage. Moreover, if the patient faints, as may occur with carotid sinus hypersensitivity, the physician is notified promptly, since the counting ceases.

Miscellaneous Drugs.—In addition to the measures mentioned above, sedation is of great value in treating serious arrhythmias. Especially when the patient is apprehensive, morphine or another equally effective sedative is indicated. These agents may serve a double purpose. They not only calm the patient but also appear to exert an antiarrhythmic effect on the heart; thus, in many instances the arrhythmia stops soon after the sedative is given.

The vast majority of urgent cardiac arrhythmias can be managed successfully by proper use of sedation, digitalis glucosides, quinidine, procaine amide, and carotid sinus massage. In exceptional instances, however, several other drugs may succeed in controlling arrhythmias that fail to respond to the commoner therapeutic measures. Among the agents that are of value under special circumstances are phenylephrine (Neo-Synephrine) hydrochloride,[15] hydroxyamphetamine (Paredrine) hydrobromide,[16] methoxyamine (Vasoxyl) hydrochloride,[17] methacholine (Mecholyl) chloride,[18] potassium salts,[19] and antihistaminics.[20]

COMMON CARDIAC ARRHYTHMIAS

Every patient with cardiac arrhythmia presents a special problem requiring individual consideration and care. Nevertheless, certain didactic rules may be given that are generally applicable in the emergency treatment of the common arrhythmias. A basic principle underlying such therapy is that the clinical severity of any arrhythmia is usually proportional to the disturbance of ventricular rate. Whether the ventricles beat too rapidly or too slowly, the gravity of the patient's condition increases as the rate deviates from the normal. Consequently, the goal of emergency treatment should always be to control the ventricular rate, even though the arrhythmia persists. For example, patients with paroxysmal auricular fibrillation often display ventricular rates of 200 per minute or more. As a result of the excessive ventricular rate, such patients are in critical condition. If rapid digitalization is carried out, the ventricular rate drops to 70 or 80 per minute and the patient presents a dramatic clinical improvement although the auricular arrhythmia persists unchanged.

Paroxysmal Auricular Tachycardia.—Severity varies in paroxysmal auricular tachycardia from a mild disorder of little consequence to a grave, or even fatal, disturbance. If the rate is slow and the paroxysm short, as occasionally happens, the arrhythmia may be asymptomatic and harmless. If the rate is extremely rapid, the tachycardia presents a serious emergency requiring prompt and effective treatment.

The typical instance of paroxysmal auricular tachycardia occurs at a pulse rate of about 160 per minute in a young or middle-aged patient with a normal heart. Carotid sinus massage often causes a dramatic cessation of the arrhythmia. If this procedure proves ineffective, a strong sedative such as 0.2 gm. of pentobarbital sodium combined with 0.4 gm. of quinidine should be given orally. The patient goes to sleep and usually awakens with normal sinus rhythm. If not, lanatoside C or ouabain should be administered intramuscularly or, with caution, intravenously. If the arrhythmia persists despite the digitalis preparations, the patient is given quinidine and/or procaine amide in large doses. As a last resort, methacholine or acetylcholine can be administered.

In elderly patients with rapid auricular tachycardia, the problem is much more serious. Carotid sinus stimulation may be hazardous.[21] Intravenous digitalis also may be dangerous, since the tachycardia may be a manifestation of underlying recent myocardial infarction with extension to the auricles. The treatment of choice in older patients would appear to be the simultaneous intramuscular administration of digitalis and quinidine. Digitalis is given because congestive heart failure may be present or impending. Shock often occurs and must be promptly combated with pressor drugs such as arterenol (norepinephrine). In elderly patients with frequently recurring paroxysms of tachycardia, digitalization has been found to be of great prophylactic value even in the absence of congestive failure.[22]

Auricular tachycardia is a grave emergency in infants as well as in elderly patients. Rapid tachycardia in infants often causes congestive failure and death. The arrhyth-

mia frequently is not recognized. Intravenous administration of digitalis is the treatment of choice in these critical cases.[23]

Auricular Flutter.—Since organic heart disease is usually present in patients with auricular flutter, treatment should be directed first toward protection of the ventricular myocardium. Digitalis is indicated if the ventricular rate is fast or if evidence of heart failure is present. Once the ventricular rate has been slowed, the emergency no longer exists. Conversion to normal sinus rhythm may then be considered. If the heart is relatively small and cardiac function is satisfactory, conversion with quinidine should be tried. If, on the other hand, the heart is greatly enlarged and congestive failure is present, an attempt to restore normal rhythm may be inadvisable. Normal ventricular rates can be maintained in these patients even though the auricular flutter continues. Attempts to convert with quinidine often cause a decrease in the degree of auriculoventricular block, with consequent increase in the ventricular rate. This hazard may be reduced by the judicious use of digitalis. If repeated paroxysms of flutter cannot be prevented with quinidine or procaine amide, the treatment of choice is digitalization to prevent rapid ventricular rates during the paroxysms. The value of such therapy is illustrated by the following case.

CASE 1.—The patient was a concert singer whose work had been severely handicapped by recurring bouts of flutter with rapid ventricular rates of around 150 per minute. These paroxysms often developed while he was singing in concerts; one such attack caused loss of consciousness during a performance. Quinidine and procaine amide were tried, but they failed to prevent the paroxysms. The patient became depressed and worried; he feared that his career was over. Subsequently digitalis was administered. Although his paroxysms of flutter still recurred during concerts, the ventricular rate remained around 90 per minute and he experienced no severe symptoms. Thus, he was able to carry on his work and resumed his concert career.

Auricular Fibrillation.—Like flutter, auricular fibrillation is an emergency when the ventricular rate is rapid. This is most often the case in paroxysmal fibrillation. The first goal of therapy, therefore, is to slow the ventricular rate by the parenteral use of digitalis. Not infrequently, fibrillation will convert to regular sinus rhythm with digitalization.[24] As long as the ventricular rate has been slowed, however, conversion is not an emergency. An exception to this rule occurs when the fibrillating auricles have thrown off emboli. A vigorous attempt at conversion should then be made, since further embolism may be prevented by restoration of sinus rhythm.[25]

If auricular fibrillation persists despite digitalization and embolism has not occurred, the problem of whether or not to attempt conversion must be considered. Considerable difference of opinion has always existed concerning this question. In general, the smaller and less diseased the heart, the greater are the chances of restoring normal rhythm. Quinidine, procaine amide, or both may be used for conversion. Procaine amide has been found especially valuable in instances of paroxysmal fibrillation.[26] Blood quinidine determinations are sometimes useful, especially when greater than average doses are administered.[27] If sinus rhythm cannot be achieved with moderate amounts of quinidine or procaine amide, it is seldom advisable to force the issue by increasing the dosage. Fibrillation frequently recurs when extremely large doses have been required to produce conversion. If the arrhythmia recurs repeatedly, as in many patients with mitral stenosis, attempts to restore sinus rhythm should be abandoned and a slow ventricular rate maintained with digitalis. The presence of hyperthyroidism, perhaps in a masked form, should be suspected and excluded in every instance of auricular fibrillation.[28]

Ventricular Tachycardia.—The serious disturbance of ventricular tachycardia usually is associated with severe organic heart disease, most commonly after recent myocardial infarction. Most instances of ventricular tachycardia therefore present grave emergencies and require prompt and vigorous treatment. The arrhythmia should be abolished as quickly as possible by the parenteral use of quinidine and/or procaine amide. While there is much more experience in the use of quinidine, evidence seems to be accumulating that procaine amide may be the drug of choice.[29] In urgent cases, as much as 1 to 2 gm. of procaine amide (10 to 20 cc. of solution) should be given intramuscularly as an initial dose.[4] Subsequent doses of 1 gm. given intramuscularly at intervals of one to three hours are sometimes necessary. When given intravenously, procaine amide appears to be safer than quinidine and possibly more effective.[8d] Either of these drugs reduces ventricular conductivity and is therefore potentially capable of producing ventricular fibrillation, especially when large doses are given. For this reason, frequent electrocardiograms should be taken during treatment.

Since ventricular tachycardia is one of the most serious of all arrhythmias, every effort must be made to prevent its occurrence. As soon as the physician observes signs of a probable attack, such as frequent ventricular extrasystoles, or if one attack has already occurred, prophylactic measures should be instituted. Procaine amide is especially valuable in preventing ventricular tachycardia. Quinidine has long been used successfully for this purpose.

Cardiac Arrest.—Impairment or stoppage of cardiac output, commonly termed "cardiac arrest," may occur in a variety of conditions including complete heart block with episodes of ventricular asystole, ventricular fibrillation, and complete cardiac standstill. Management of these conditions is often difficult, since usual methods of therapy frequently fail to restore normal rhythm. Special treatment must then be improvised if the patient is to survive.

The treatment of asystole with syncopal attacks in patients with complete heart block consists of the administration of epinephrine. If attacks recur, repeated injections of epinephrine or the longer-acting epinephrine in oil suspension are required. Episodes of ventricular asystole may be prevented by isopropylarterenol (Isuprel) hydrochloride in doses of 10 to 15 mg. sublingually or hydroxyamphetamine in doses of 20 to 60 mg. orally at three to four hour intervals.[30] Since routine drugs often prove ineffective, more specialized therapy is often re-

quired to restore normal rhythm. This principle is illustrated by the following case in which attacks of syncope resulting from asystole were terminated by means of corticotropin (ACTH).

CASE 2.—After a posterior myocardial infarction, complete auriculoventricular heart block with attacks of asystole developed in a 60-year-old man. Severe syncopal attacks, causing loss of consciousness for several minutes, occurred many times a day. These attacks continued for a week despite increasing doses of isopropylarterenol, epinephrine, hydroxyamphetamine, ephedrine, and atropine. Several episodes lasted so long that death seemed imminent. Finally, in desperation, 40 mg. of corticotropin was given. The rationale of this treatment was as follows: Complete heart block following myocardial infarction is not always due to permanent and complete destruction of the auriculoventricular node and bundle of His. Instead, these regions may merely be involved by an inflammatory reaction at the edges of the infarct. Under such circumstances, corticotropin may suppress the inflammation and thereby abolish the block. Apparently this occurred in the present instance, for the heart block disappeared a few hours after corticotropin was given (fig. 1). Normal sinus rhythm then persisted for several days; then complete heart block suddenly recurred. Severe and

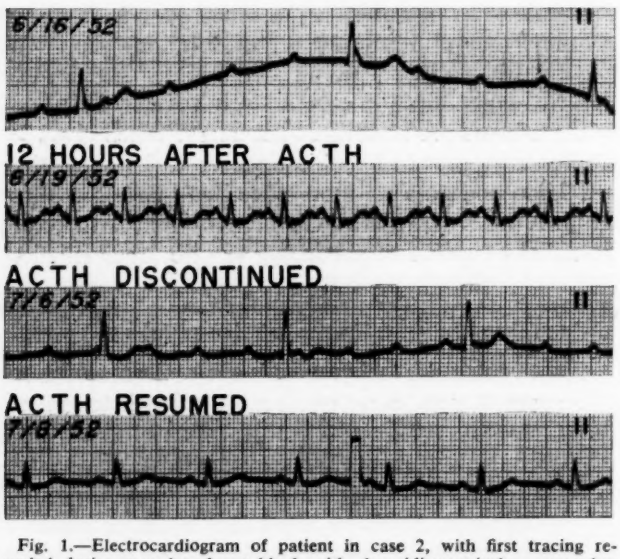

Fig. 1.—Electrocardiogram of patient in case 2, with first tracing recorded during complete heart block with slow idioventricular pacemaker following posterior myocardial infarction. After a week during which conventional therapy failed to control such attacks, corticotropin (ACTH) was given. Second tracing made 12 hours after initial dose of corticotropin shows normal rhythm. Two weeks later, heart block returned (third tracing) and persisted despite conventional therapy until corticotropin was given (fourth tracing). Apparently the heart block was due to temporary inflammation and edema of auriculoventricular node and bundle of His that was suppressed by corticotropin.

frequent attacks of syncope again ensued and again could not be controlled with the usual drugs. A second dose of corticotropin was given. For the second time, the block was abolished almost immediately. Corticotropin was administered for 10 days and then discontinued. The block did not recur and the patient experienced no subsequent syncopal attacks.

Thus on two occasions, heart block that had been present constantly for several days and that did not respond to the usual treatment, disappeared promptly after administration of corticotropin. Such prompt changes could hardly have been a coincidence. Evidently the auriculoventricular node and bundle of His had been edematous and inflamed during the acute stage of infarction. This acute condition that caused the block was suppressed by corticotropin. Similar treatment with corticotropin may aid in other instances of temporary heart block following infarction that is refractory to more conventional therapy. If the block is due to permanent pathological changes, of course, corticotropin will be of no avail.

Patients with complete heart block may have syncopal attacks as a result of paroxysmal ventricular fibrillation rather than asystole. Since such attacks are extremely difficult to terminate, therapy must be concerned chiefly with preventing the paroxysms of fibrillation. Atropine given intravenously in doses of 2 mg. occasionally may be effective in aborting the syncopal attack.[31] Isopropylarterenol and hydroxyamphetamine may prevent episodes of ventricular fibrillation by accelerating the basic idioventricular rate.[30] Quinidine and procaine amide are definitely contraindicated, as they have been known to induce ventricular fibrillation in the presence of complete heart block by depressing the basic idioventricular pacemaker.[32] In patients with previously normal auriculoventricular conduction, on the other hand, procaine amide or quinidine given intravenously is the treatment of choice for ventricular fibrillation.[30] These drugs enable the sino-auricular node to recover its pacemaking function and normal sinus rhythm supervenes as in the successful treatment of ventricular tachycardia.

Syncopal attacks resulting from cardiac asystole due to carotid sinus hypersensitivity usually are treated by the same methods as complete heart block with ventricular asystole. Unfortunately, routine drugs frequently fail to control these attacks. A useful approach in certain such instances is suggested by the specially devised therapy used in the following two cases.

CASE 3.—A 65-year-old woman suffered innumerable syncopal attacks due to ventricular asystole resulting from carotid sinus hypersensitivity. The slightest stimulus, such as swallowing or light external pressure applied to the carotid sinus, produced asystole. Even when the patient was hospitalized, these attacks continued with incapacitating frequency. Routine drugs, including epinephrine, hydroxyamphetamine and atropine, proved ineffective. Denervation of the carotid sinus was finally proposed. As the patient was being prepared for surgery, however, a severe attack occurred and necessitated abandonment of the operation.

After all other measures had failed, the patient was given large doses of thyroid hormone to accelerate the heart. When a state of mild hyperthyroidism had been produced, the heart rate increased and the episodes of asystole and syncope ceased. Mild hyperthyroidism was maintained with thyroid medication for several months, during which time the syncope did not recur.

Thus, the production of mild thyrotoxicosis transformed an incapacitated patient into an active woman. This appears to be a new example of substituting a benign disease for a more serious one. The case is merely suggestive, however, since carotid sinus hypersensitivity often disappears spontaneously.

The successful use of thyroid hormone to prevent syncopal attacks was further suggested by recent experience with a patient who had complete heart block. Despite routine drugs, such as isopropylarterenol, the patient had frequent incapacitating episodes of syncope. Thyroid hormone was finally prescribed in doses sufficient to elevate the basal metabolic rate and blood iodine level from low normal to high normal values. Thyrotoxicosis was not induced in this instance, the blood iodine level being changed from 4 mcg. to 6.6 mcg. During the six month period after thyroid therapy was instituted, the

ventricular rate was faster and no syncopal episodes occurred. As in case 3, however, whether the syncope ceased spontaneously or as a direct result of the thyroid therapy cannot be definitely established.

Largely because of certain dramatic surgical procedures, a growing interest recently has been shown in the treatment of cardiac standstill and of ventricular fibrillation. Failure of the ventricles to eject blood, as a result of either standstill or fibrillation, requires immediate and drastic therapeutic measures. The cells of the cerebral cortex may undergo irreparable damage unless circulation can be restored within three to four minutes. The external electric stimulator, a device that serves as cardiac pacemaker, has been used successfully in certain instances of ventricular standstill.[33] Direct cardiac massage may be lifesaving in either cardiac standstill or ventricular fibrillation.[34] The technique consists of manual compression of the heart at a rate of 80 to 120 times per minute. Venous return to the heart should be supplemented by rapid intravenous transfusion of blood. The patient is placed in the Trendelenberg position, and intermittent occlusion of the thoracic aorta is carried out in order to increase the blood flow to the brain and coronary arteries. When administered for cardiac standstill, massage should be continued for at least one hour unless spontaneous contractions are observed sooner. From 2 to 4 cc. of 10% calcium chloride or 0.1 to 0.3 cc. of 1 in 1,000 epinephrine in 5 cc. of isotonic sodium chloride may be injected into the left ventricular cavity to augment the effect of massage.[35] In instances of ventricular fibrillation, cardiac massage must be continued at least until the heart is well oxygenated. While massage is in progress, 5 cc. of 2% procaine is injected into the pericardial sac and procaine amide is given intravenously. Ventricular fibrillation rarely will be converted to normal sinus rhythm by these measures alone. In the majority of cases, an electric defibrillator must be used after oxygenation of the heart has been achieved by massage.[36]

The preceding discussion emphasizes the futility of treating all cardiac arrhythmias according to a fixed set of rules. Optimal results can be achieved only if the physician remembers that he is dealing with a patient rather than an arrhythmia. As in the following case, specially designed therapy, based on an evaluation of the patient's history and the total clinical picture, may succeed when routine antiarrhythmic measures have failed.

CASE 4.—A middle-aged man without evidence of organic heart disease had suffered from gout for several years. This patient's heart had persistent bigeminal rhythm, every second beat being a ventricular extrasystole (fig. 2). Arrhythmia became so troublesome that it interfered with his work. Quinidine and procaine amide were given a thorough trial but failed to affect the disturbance. Because of the possibility that the ventricular focus might be a microscopic gouty deposit, the patient was given probenecid (Benemid), a drug that increases the excretion of uric acid.[37] After adequate doses of probenecid, the bigeminy disappeared. When the drug was withheld, coupling returned.

The effectiveness of probenecid, in this instance suggests that similar treatment may be worthy of trial in other patients with gout who present ventricular extrasystoles.

SUMMARY AND CONCLUSIONS

The majority of cardiac arrhythmias can be controlled by proper use of the digitalis glucosides, quinidine, procaine amide (Pronestyl), carotid sinus massage, and sedation. Since the clinical severity of an arrhythmia is usually proportional to the disturbance in ventricular rate, emergency treatment is designed to normalize this rate even though the arrhythmia persists. Paroxysmal auricular tachycardia frequently can be terminated by carotid sinus massage. This arrhythmia presents a grave emergency if the rate is extremely rapid. Rapid-rate auricular tachycardia in elderly patients should be treated with digitalis and quinidine given intramuscularly. Rapid auricular tachycardia in infants may cause congestive failure and requires immediate intravenous administration of digitalis. Since auricular flutter usually is associated with organic heart disease, digitalis is indicated if the ventricular rate is rapid or if evidence of heart failure is present. Conversion to sinus rhythm is not essential, provided the ventricular rate has been slowed. Auricular fibrillation with rapid ventricular rates is treated by parenteral administration of digitalis. Attempts to induce conversion with quinidine and/or procaine amide may be advisable in certain instances. Ventricular tachycardia is one of the most serious cardiac arrhythmias, requiring prompt and vigorous therapy. Parenteral administration of quinidine and/or procaine amide is the treatment of choice. The management of cardiac arrest is extremely difficult, since many patients fail to respond to routine therapeutic measures. Epinephrine, isopropylarterenol (Isuprel) hydrochloride, and hydroxyamphetamine (Paredrine) hydrobromide may be useful in treating syncopal attacks resulting from asystole in patients with complete heart block or with carotid sinus hypersensitivity. Syncopal attacks resulting from paroxysmal ventricular fibrillation in patients with complete heart block occasionally can be terminated with atropine or prevented with isopropylarterenol and hydroxyamphetamine. Quinidine and procaine amide are contraindicated if heart block is present, but these may be used to control paroxysms of ventricular fibrillation in patients with previously normal auriculoventricular conduction. Failure of the heart to eject blood, as a result of either cardiac standstill or ventricular fibrillation, may cause permanent damage to the cerebral

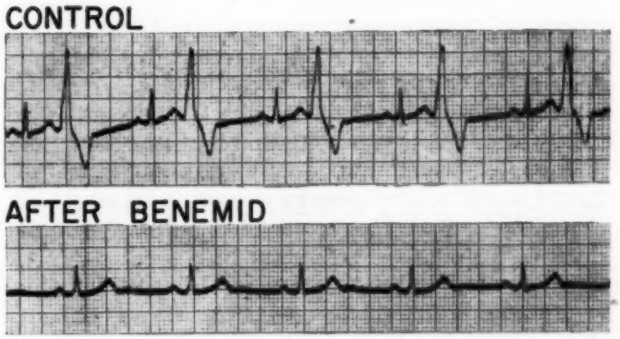

Fig. 2.—Electrocardiogram of patient with gout (case 4), before and after administration of probenecid (Benemid). Control tracing shows bigeminal rhythm with every second beat a ventricular extrasystole. The extrasystoles disappeared after probenecid was given (bottom tracing) but returned when the drug was withheld. This sequence of events suggested the possibility that the ventricular focus may have been a microscopic uric acid deposit.

cortex within three to four minutes. Lifesaving measures in cases of cardiac standstill are the use of the external electric stimulator and direct cardiac massage. In ventricular fibrillation, the heart may be oxygenated by direct cardiac massage, after which an electric defibrillator is used to restore sinus rhythm. Among the several reports of cases illustrating the need for specially devised therapy in patients who fail to respond to routine antiarrhythmic measures, one case concerns the successful use of corticotropin (ACTH) to terminate heart block following myocardial infarction. Corticotropin should be tried in such instances when usual methods of therapy fail, as the heart block may be due to inflammation of the auriculoventricular node and bundle of His, which can be suppressed with the drug.

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PSYCHIATRIC OBSERVATIONS IN NEUROCIRCULATORY ASTHENIA

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Anxiety is a phenomenon that is so common, and yet so hard to define clearly,[1] that when an opportunity comes to study any part of the total phenomenon in a more or less pure form, it is worth while to take advantage of it. Such an opportunity exists in the case of the effort syndrome [2] (or neurocirculatory asthenia [3]), in which the physiological components of anxiety are the chief symptoms. Even though some patients may not complain that they are anxious, the well-known somatic symptoms of anxiety are present in this condition along with apprehension, fear, and nervousness that occur at rest, on effort, or as a reaction to excitement.

Neurocirculatory asthenia or effort syndrome is a common condition that has especial interest because of its close resemblance to anxiety neurosis [4]—or to use the older term, neurasthenia or nervous exhaustion. It is characterized by ". . . a combination of symptoms —dyspnea, palpitation, precordial pain or discomfort, easy exhaustion, and faintness too readily induced by effort or excitement or even coming on at rest, without evidence of heart, lung, or brain disease." [4b] Close study of patients reveals that there are usually many symptoms in systems other than the circulatory, e. g., dizzy spells, tinnitus, nervous "chills," sighing respirations, insomnia, "nervous" feelings, and many others.[4b] All these symptoms may also come on at rest, as in the classical anxiety neurosis. A great many studies have been done on this disorder, especially because of the military importance, i. e., it tends to appear under conditions of military life. Much has been learned concerning the various symptoms, their relation to other psychiatric conditions,[5] the prognosis or natural history, cardiovascular functions,[6] and the difference from ordinary fear of external origin.[5]

As a result of these many investigations, it may now be said that this condition is a form of anxiety neurosis in which the effort of physical exertion has become an important precipitant. It is known that this is a symptom-complex occurring in a variety of mental illnesses [5] such as hysteria, neurotic depressions, and even schizophrenia. For instance, there is a reference to it in Schreber's history as quoted by Katan [8]: "Another symptom which we must now consider (and one which was present in both illnesses) is oppression of the heart. This symptom became so intense that even walking on a moderately rising slope caused anxiety attacks." Here it was a phobic reaction to the danger of meeting temptations of a homosexual sort.

It is known that the condition may be acute but that in some cases it can become a chronic, disabling condition requiring the patient to modify his life in order to avoid stresses. Even when the patient does not complain primarily of intolerance to effort, his performance and work tests are not normal, and all patients have a decrease in efficiency.[9]

Miles and Cobb [10] have brought out that it is illogical to make a separate disorder of this symptom-complex, and they cite a number of instances in which the cardiovascular-respiratory symptoms are present in cases of psychoneuroses, such as hysteria, hypochondriasis, and obsessional neurosis; they are recognizable by the psychiatrist but not easy for the internist to understand because of his greater emphasis upon somatic symptoms. They point to the error that will result if all such diverse conditions are considered to be the same merely on the basis of the somatic symptoms they have in common.

The etiology of the disorder has not yet been clearly defined, i. e., whether it is psychogenic in the manner of a hysterical symptom or a phobia or whether some

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chemical or other biological factor is set off by psychic influences. For instance, a high family prevalence can be shown,[11] though the significance of this is unknown. Whether it means a hereditary etiology, or a learned pattern, or a combination of the two, has not been determined. Psychiatrists in recent decades have not been generally interested in this condition as a separate phenomenon. It is the internists who have been mainly concerned with it. One modern view among medical investigators [12] is to regard this disorder "not as a permanent or fixed disease entity, but as a circulatory disorder which may fluctuate widely in any one individual. . . ." In other words, it occurs in normal persons also under certain environmental stresses. Certainly anyone treating psychiatric patients will have observed such fluctuations in the somatic symptoms during treatment. Freud's early description of the anxiety neurosis [4a] showed his interest and is still the best clinical description of its symptomatology, but the psychoanalysts have not devoted as much attention to it as to most aspects of mental disorder, preferring to regard it simply as a somatic component of anxiety.

In the clinical practice of psychiatry it is not seen commonly, as many patients respond favorably to reassurance and simple explanation by a medical man, and only the worst cases are seen by psychiatrists. The severer cases, in which there are severer psychoneurotic disorders, and patients who do not respond to this simple treatment are often seen years after the onset by a psychiatrist, if the patients seek psychiatric help at all. Many of these patients have severe agoraphobia and cannot go out into the street without great anxiety, much less indulge in strenuous effort. Recently a paper by Blau [13] and one by Brenner [14] suggested a revival of interest among psychoanalysts in this disorder, which has been called an actual neurosis as opposed to a psychoneurosis, meaning that a somatic etiology, as yet undiscovered, is present as part of the neurotic process.

Wood and his co-workers in England have come close to a completely psychological formulation.[15] They found psychological symptoms present in all cases and concluded that "effort syndrome is a disorder found in various psychiatric diseases, that it is a manifestation of the anxiety state and not a separate disorder in itself." Unfortunately this does not define its position in the neuroses.

Lewis [2] observed the psychological irregularities and said that a certain number of patients were "neurasthenic, of highly strung temperament, a number sensitive or querulous, others apathetic or depressed." He saw among them many "minor phobias," such as fear of the dark, and added that "some were not of the average normal sexually." There were "hysterical breathlessness and fainting attacks of frankly hysterical nature."

A more specific psychological viewpoint has been given by Dunn,[16] who said that this disorder shows conflict arising from a precipitating situation in life and a predisposing factor of some kind, manifested by a failure to adjust to society in some of its forms, e. g., games and sports. Whether this comes from a familial constitutional tendency or from fear and anxiety acquired in childhood is not certain. Dunn stated that frequently the patients have been "conditioned to alarm" about their hearts early in life and have a tendency to focus symptoms about that organ when later conflict develops.

The formulation of Miles and Cobb [10] gives a basis for understanding the diverse nature of cases that have these symptoms in common. They state that there is more than one etiological factor concerned, that psychogenic as well as genogenic (constitutional) influences are at work, in different proportions in different cases. This formulation opens the possibility for further investigation, allowing one to consider: 1. What are the psychogenic factors? 2. What is the interplay between psychogenic and constitutional factors?

It is with these two questions that this article is concerned. What, if any, specificity is there in the nature of the predisposition from the psychological viewpoint? Particularly, what are the conditions under which it can become fixed in a chronic state so that the patient becomes a partial invalid? While it is true that anxiety can lower exercise tolerance even in normal persons temporarily, what is the mechanism that lowers work efficiency continuously, creating a lasting state of circulatory inefficiency?

In order to define this condition more clearly, a group of soldiers with neurocirculatory asthenia, who formed the basis for studies of physiological observations,[17] were questioned in a controlled interview as to the presence of certain symptoms in their lives. The results were compared with those in a group of normal soldiers of comparable age group who were similarly examined. In the discussion that follows the terms effort syndrome and neurocirculatory asthenia are used interchangeably.

METHOD

The patients were enlisted men (mainly drafted) taken from the medical and psychiatric wards of military hospitals during World War II. It should be emphasized that they were selected for their physiological complaints alone, i. e., palpitation or rapid heart rate, shortness of breath or breathing discomfort, pain in the chest, and dizziness or faintness upon effort and excitement. They were examined carefully to exclude other systemic diseases.

A questionnaire of neurotic symptoms, the Minnesota Multiphasic Personality Inventory, had previously been given to a group of these patients and to normal control subjects. It was found [4b] that, whereas the normal subjects had normal scores on this test, the patients had high scores in hypochondriasis, depression, and hysteria and scores somewhat elevated above the normal average in psychasthenia (phobias). To check this, and also to enlarge on the findings, psychiatric interviews were held with the patients, as follows:

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16. Dunn, W. H.: Emotional Factors in Neurocirculatory Asthenia, Psychosom. Med. **4**: 333-354 (Oct.) 1942.
17. White.[4b] Cohen.[6] Cobb.[6]

A controlled interview was held with each patient, a questionnaire being filled out by the examiner during the interview covering 140 items dealing with present symptoms, past history, and family history. Included also were a number of questions about fears, phobias, anxieties, obsessions, and compulsions. Some of the patients were interviewed many times in an attempt to obtain more detailed personal histories, but most of the information tabulated and used in this quantitative study was obtained in the initial interview, so that the results are not distorted by the fact that some patients were observed for longer periods than others. The men in the control group were all seen once or twice and interviewed in the same manner. The control group consisted of 55 young combat military police who had finished their basic training and were prepared for foreign duty. None had been hospitalized, and they were supposed to be as normal and symptomless a group of enlisted men as could be provided by the Army.

The cases of neurocirculatory asthenia were divided arbitrarily into two groups: 1. The first group comprised 32 persons with acute neurocirculatory asthenia who had been well at one time in the past and who remembered the beginning of their trouble, including 20 who broke down in combat, 6 in military service but not in combat, and 6 before entering military service. 2. The second group comprised 79 patients with chronic neurocirculatory asthenia. These patients had had some degree of invalidism from these symptoms for as long as they could remember.

Certain purely psychic symptoms were found to be present. These symptoms may be divided into four groups of classical psychoneurotic symptoms: (1) phobic, (2) depressive, (3) hypochondriacal, and (4) hysterical.

PHOBIC SYMPTOMS

The patients with chronic neurocirculatory asthenia (anxiety neurosis) showed a high number of fears and phobias, most of them not obviously crippling. Among patients with the chronic form, 89.8% had phobic symptoms; among those with the acute form, 75% had such symptoms; and among the normal subjects, 32% had them.

There is a strong contrast also among the three groups regarding quality as well as quantity. Many more of the patients in the chronic group had developed avoidance reactions such as never traveling by train or bus and not taking elevators or subways. In addition, a larger number of this group were generally fearful or timid persons. The few symptoms that the normal control subjects had were milder, less crippling, and more confined to minor situations or those where reality enters, e. g., "doesn't like to go too close to the edge" in high places or "doesn't like snakes." The group of patients with chronic complaints contained many who said that all their lives they had avoided certain things. In the group of patients with acute symptoms of anxiety neurosis, there were some who early in life had phobic symptoms preceding by years the development of the characteristic symptoms of neurocirculatory asthenia, including fear of death and bodily injury.

Among the acute cases there was superficially much less tendency to be fearful, and the men were superficially more active and aggressive. However, the impression from this study is that there was either an undercurrent of anxiety or a residue of some latent, long-standing anxiety that could be activated under certain circumstances. In most of the chronic cases, on the other hand, this anxiety was not latent but manifest, and many of the chronic cases could have been detected at induction centers. The incidence in the control group, 25%, as well as the well-known fact that relatively normal persons have minor phobias and avoidances, shows that certainly not all persons with phobias have neurocirculatory asthenia.

In conclusion, it may be said that most patients with this type of anxiety neurosis have a phobic neurosis of some proportions. Furthermore, this becomes in many cases a phobic attitude toward making effort and taking physical exercise. During an attempt to train these men with a trainer who gave graduated conditioning exercises, it was observed that the patients' attitudes were as remarkable as their exercise intolerance; they were resistant, lethargic, moody, irritable and fearful and gave the impression not of extending themselves but of holding back, as though from a frightening ordeal. It was more than a simple limitation of exercise tolerance, it was also a severe resistance to being subjected to the test and the training procedures. It seemed that the exercise itself had become the phobic object, and upon exposure to it, the patients' anxiety increased greatly.

DEPRESSIVE SYMPTOMS

There were several symptoms usually seen in depressions of a neurotic nature, including anorexia, insomnia, unhappiness, nervousness, and irritability. One could add that such patients are "tired all the time," effort is a great burden, ambition is poor, and morale is low. There is no crying or any of the guilt feelings of melancholia, but rather unhappiness with their lot. They do not feel guilty, but put upon and resentful.

HYPOCHONDRIACAL ELEMENT

Many of the patients in this study felt that they had heart disease and that they should not be forced to do the same kind of work that others did. This feeling is based upon a strong hypochondriacal component, revealed by excessive self-observation, worry about health at the time of induction, consideration of self as too ill for full duty at time of induction, thoughts of not being well enough in service, and thoughts of having once been warned by a doctor to take life easy or of heart disease. These findings suggest a preoccupation with health, although the way in which it came about is not explained, so that further examination is necessary to ascertain the presence and degree of fixity of certain hypochondriacal ideas.

Forty patients and 53 control subjects were interviewed with a questionnaire in which they were asked to tell what they thought was the matter with them under four headings: 1. Is anything wrong with your nerves or emotions? 2. Is anything wrong with your heart? 3. Is anything wrong with your other organs? 4. Can you

get well? Thirty of the 40 sick men and only 2 of the 53 control subjects thought they had something wrong with their "nerves or emotions."

Twenty-seven of the 40 thought it was heart disease of some sort, with such remarks as "Heart trouble. Never believe doctors. When your number is up, your number is up." "I think there is really something there. Don't believe it is a disease." "It may be a sickness I can't get over." The intensity with which the patient hung on to his symptoms was suggestive of a defensive reaction, i. e., he did not want to lose the symptom, rather than that he welcomed a chance to talk about getting rid of it. Of the 40 patients, 20 thought that some other organ was involved, e. g., "might get a stroke" or "lungs ruined by cough." In some of these instances the stomach was thought to be involved.

Twenty-two of the 40 patients, and one of the 53 control subjects, thought they could not get well. "It's a chronic case, the doctors say," one man commented. Many thought that if they could get out of the military service they could get well or be able to live as before, so that they would at least be spared very severe symptoms.

MECHANISMS OF SYMPTOM FORMATION

To determine the degree of fixity of the conviction of heart disease, more details are needed. In cases in which frequent interviews were held, there is some additional information that at least gives an impression as to how the body is involved in the patient's thinking and feeling, as well as to how the phobic element may fit into the life pattern. The following two cases are illustrative.

REPORTS OF CASES

CASE 1.—The chief complaint was heart pain and dizziness on exertion for many years. The patient had had to "take life easy" since childhood and avoided exercise for years because of palpitation, dizziness, trembling, weakness, and general discomfort. He was a skilled worker in a factory but had to do light work, e. g., he could not work overtime and was unable to engage in dancing because he became dizzy too easily on fast numbers and perspired heavily when under tension or in a warm room. Indoors in crowds he sometimes experienced the same symptoms, even without exertion.

He seldom had clear-cut attacks of anxiety, perhaps because he was usually able to avoid anxiety-producing situations. For example, he never went into high places and avoided elevators whenever possible because he became uncomfortable in them. He fainted when getting his immunization shots at the time of induction. During basic training he broke down and reported sick because he could not stand the long hikes with heavy pack.

In the course of several interviews it was discovered that actually the first symptoms occurred at the age of 6, when his mother died of a cerebral hemorrhage. After this he felt "feeble and inactive," wanted to avoid people, and did not feel like doing "anything strenuous." The father was a brutal alcoholic who beat the children. The patient did not want to play with other children, preferring to stay inside and read his books at recess time. When he did attempt to join in the games, he found that he was awkward, and the teacher often had to force the other boys to take him on their side. Finally, after suffering this anxiety upon contact with other boys, he prevailed upon the family doctor to have him excused from exercises and games because of alleged weakness of the heart. Since then he had taken life easy and had noticed that exercise gave him these typical symptoms.

At the age of 16, when hurrying one day after church, he had a pain in the chest that he thought was due to the heart, as it had become a fixed conviction that this organ was defective. What had begun as a difficulty in social adaptation was now changed, with the help of the physician, into a so-called "weak heart." The little boy, helpless to overcome his difficulties in taking his place among his fellows, competing and fighting, had been provided with a protective device that made it unnecessary for him to compete. From the beginning there had been the wish to keep away from competition and association with other boys. The motive behind this feeling of inadequacy—whether a feeling of femininity or passivity or an aggressive excitement too great to deal with—is not clear.

When he first took gymnastic classes in school, he was fat, bowlegged, and awkward. He would come up to the high jump and be "frozen in my tracks. It was too high. Something made me stop." This is suggestive of the cases reported by Duncan,[18] in which exercise tolerance was lowered when the patient was confronted with a task at which he thought he would fail. However, at some exercises he was good. He failed only at those to which some fear was attached; e. g., competitive games at which he was awkward and in which the other boys got angry if he was on their side. The teacher would say, "Go ahead, take him on your team." Eventually he managed to get excused from gymnasium work. It was several years later that he noticed shortness of breath. Anxiety initially occurring in relation to interpersonal difficulties was turned toward the body, and its meaning was reinforced by some warnings from doctors.

In his military outfit the patient felt inferior and insecure. "I felt awkward. I was not as well built as they were. I thought —what is to become of me?" He was a "questionable inductee," and heart and blood pressure were examined twice before he was accepted. When his outfit was formed, he had the "two meanest corporals" who were "disliked by everyone." In this setting he broke down, ostensibly from walking three miles with a 60 lb. (27.3 kg.) pack, but one wonders whether his anxiety about the "two meanest corporals" was not a motivating factor. His powerlessness in the face of odds took the form of excessive fatigue upon exercise and marked heart consciousness perhaps resulting from his anxiety over his own passivity.

This brings in another aspect of his personality that gave him difficulty, namely, his fear of bodily injury related to his identification with his mother. He wanted to take especially good care of himself because he feared that, like his mother, he would die before his time. He said that he looked older than he was, that he was wearing himself out early and getting old before his time. He avoided accidents, effort, and danger because of the fear of getting hurt. Whereas the rest of his family were careless, he was careful, e. g., he suggested several safety devices for his factory, of which three were adopted. These were all methods of keeping persons from being injured or trapped.

The sexual history also brings out the way in which his defenses operated to protect himself from harm. He was always very shy with girls, partly because of acne, and he married the first girl he kissed. His wife, who was large and capable, really married him, he stated. It happened that he wanted to leave home and marriage was an excuse. It was actually her idea that they marry. He had engaged in masturbation before marriage but had had no sexual relations. He added that by marrying he was able to get away from home, where he had too much responsibility for his alcoholic father. The wife was a protection against his fear of being too intimately concerned with his father. To put it another way, a strong passive trend was present in his relations to both women and men, although with men it took the form of avoiding personal contact.

Other patients were seen who had somewhat similar mechanisms, where normal somatic reactions became a point of displacement for psychic conflicts. An example follows.

18. Duncan, C. H.; Stevenson, I. P., and Wolff, H. G.: Life Situations, Emotions, and Exercise Tolerance, Psychosom. Med. **13**: 36-50 (Jan.-Feb.) 1951.

CASE 2.—The patient was sent to the hospital because of pounding of the heart while walking from the railroad station to the reception center at camp, even before he was in uniform. He had many other symptoms. It was discovered in the hospital that since the age of 16 he had suffered some degree of incapacity because of dizziness, palpitation, fatigue, weakness, and shortness of breath upon effort or excitement. Actually some disability began at the age of 6, when he burned his feet and had to keep off them for a long time. Concurrently the father died of tuberculosis. The patient noticed when he returned to activities he could not keep up with the other boys very well, although he was able to do hard work if he took it slowly.

With the onset of more marked symptoms, he was worried about masturbation and went to his doctor because he had had many warnings from his mother that masturbation was bad. The doctor reassured him that he had not injured himself as he had feared. He was married at 19 and was warned by the doctor not to have intercourse too often because of his health. Coitus interruptus was practiced.

This is another case in which what seems like an expected degree of convalescent incapacity started the illness in childhood. What child who has been kept off his feet for weeks would not experience some results of the lack of physical conditioning when he first returns to activity? Again it seems as if some other conflict were displaced to the body, resulting in preoccupation with bodily health, a preoccupation made possible by emphasis upon the body and by the death of the father. Upon this background the later anxiety about masturbation had a point of displacement, and thereupon the illness began.

COMMENT

From the data presented it may be seen that most (perhaps all) cases of effort syndrome include some psychoneurotic symptoms. These findings are in agreement with those of most students of the subject. Wood,[5] an internist who saw several hundred cases, has said that the effort syndrome is always a part of a psychoneurosis. It may be added further that these patients are primarily phobic persons, with or without fully developed phobias, who have a hysterical capacity for investing somatic symptoms with great interest (conversion) and who have acquired a hypochondriacal attitude toward these physical symptoms. The process seems to occur stepwise, as follows:

1. The patient has at some time been impressed with a sense of powerlessness in the face of environmental forces and with a need to be passive before them. This passivity may be unconscious, and the person may even display a façade of an active, aggressive personality that overcomes obstacles actively, as is true of many patients with the acute form of the disorder. 2. A situation exists that mobilizes or stimulates this sense of powerlessness, such as training under a strict military situation. Anxiety, with its usual physiological components, occurs. 3. A body consciousness arises on which the somatic reaction makes a profound impression. 4. A displacement occurs of the patient's conscious interest and attention to the somatic symptom, with a resultant loss of interest and attention to the conflict situation, which thus becomes or remains unconscious, in the manner of hysteria. 5. The entire situation becomes fixed in this arrangement of psychic forces, creating a chronic, self-perpetuating constellation in which the patient's belief that he has bodily weakness prevents him from participating in competitive activities; the passive life fostered by such a belief leads to more feeling of weakness and more anxiety; and the process starts all over again. All degrees of this hypochondriacal fixation were seen in the patients studied: some in status nascendi and others fully developed and fixed.

This observation allows a classification to be made other than the historical one of acute and chronic, namely, one based on the extent to which the idea has developed that there is somatic disease. The patients can be separated into two groups: those with a defensive insistence on the existence of a somatic disease and those without such hypochondriacal fixation. Jones and Scarisbrick made a similar classification on the basis of their studies.[15]

The libidinal forces at work cannot be fully evaluated by this method of collecting data, but from a few cases in which the patient was known more intimately it was possible to obtain some suggestive information pointing to two additional factors: 1. An unconscious homosexual complex may exist in some patients that gives force to the passivity. 2. When either this complex or the external threats become too strong, the individual develops a sense of hopelessness, from which his symptoms grow. A study of these two factors will be made separately.

The failure of some physicians to see the psychic factors has led them to errors of oversimplification such as grouping together all patients who have the somatic symptoms of anxiety. This material verifies and expands the work of Duncan,[18] Miles and Cobb,[10] and Jones and Scarisbrick,[15] who have shown the variety and complexity of mental phenomena of which anxiety is a part.

SUMMARY

A study has been made of the psychoneurotic components of neurocirculatory asthenia (which is also known as the effort syndrome, anxiety neurosis, and neurasthenia). Although the patients were selected exclusively for physiological symptoms commonly present in anxiety, all were found to have psychoneurotic symptoms. There are three major psychological trends in the group as a whole and in varying degrees in the individuals: a phobic trend, a hysterical trend allowing displacement of interest to the body (conversion), and a hypochondriacal trend manifested by a preoccupation with the bodily symptoms. The bodily symptoms function secondarily as a defense against the feared activity, i. e., physical exercise in some cases and return to military duty in others. The core of anxiety itself seems to arise when the individual is placed in a situation that evokes a previous anxiety over being helpless in the face of outside forces that awaken a passive attitude. The effort syndrome is seen then, not as a separate disorder, but as a component of anxiety occurring where the physical effort itself, at least in some cases, has become a phobic object—a point of displacement of an unconscious conflict.

THE CARRIER STATE IN VIRAL HEPATITIS

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VIRAL HEPATITIS B

Although considerable presumptive evidence concerning carriers of hepatitis virus B (serum hepatitis virus) can be seen in retrospect to have accumulated since 1920, when Stokes and others [1] suggested that an infectious agent was responsible for liver injury following parenteral injections of bismuth or arsenicals in the treatment of syphilis, it was not until Findlay and MacCallum,[2] J. P. Fox and others (1942), and the armed services, during World War II, used yellow fever vaccine buffered with human serum [3] that striking evidence was obtained of the presence of carriers of this virus in the general population. Additional data, accumulated in England from studies on serum pools used in measles prophylaxis [4] and in the United States from experience gained with American National Red Cross plasma pools,[5] have suggested that a considerable proportion, probably 0.2 to 0.5%, of the general population carry hepatitis virus B in their blood.

Although man is the only animal known in which recognizable infection owing to this virus is capable of developing, it has not been feasible to study samples of the general population in order to determine the carrier rate with accuracy. In a number of instances, on the other hand, it has been possible to identify in retrospect blood donors who appear to be carriers by virtue of the development of hepatitis in recipients of their blood. Such evidence, however, must be regarded as circumstantial, since other modes of infection with the viruses of both hepatitis A and hepatitis B are available to most patients receiving hospital care. These include possible prior injections of other blood products, intramuscular or intravenous injections with potentially contaminated needles or syringes, and incidental exposures to hepatitis A. Thus, it is only after such circumstantial evidence has been confirmed by the actual injection of the suspected donor's blood into volunteers, with subsequent development of hepatitis in the latter, that the presence of a carrier state in the donor can be considered as established. This report concerns the retrospective detection of three such donor-carriers in this way.

Clinical Observations in Case 1.—In September, 1948, a 50-year-old white woman was admitted to the medical ward of the Albert Einstein Medical Center, Northern Division, of Philadelphia (service of Dr. Harold L. Goldburgh) because of hepatitis with jaundice that developed about six weeks after a single blood transfusion. The donor of this blood was found to have served also as one of several blood donors for another patient in whom hepatitis with jaundice developed and who had been treated at the same hospital one year previously.

The donor, W. L., was a 44-year-old white man who worked occasionally as a bar-room attendant. He was a confirmed alcoholic who for many years had consumed approximately one quart of whisky plus liberal "chasers" of beer and wine each day. This liquor consumption was frequently at the expense of food. Apart from alcoholism, his past health appeared to have been excellent; there was no history of jaundice, right upper quadrant pain, or significant gastrointestinal symptoms. He denied receiving any immunizing or other injections in recent years. By reason of having type O, Rh-negative blood, he had been called on to donate blood frequently in many hospitals in the Philadelphia metropolitan area during the previous 10 years. He maintained that he had never been rejected as a donor because of illness or untoward reactions in the recipients of his blood.

Examination of this man revealed an enlarged liver, the soft edge of which extended approximately 3 cm. below the right costal margin on deep inspiration. There were no other significant findings. Complete blood cell count, urinalysis, and blood sugar and blood urea nitrogen determinations were all normal. Liver function tests disclosed abnormalities as shown in table 1.

Aspiration biopsy of the liver on Jan. 1, 1949, disclosed considerable periportal fibrosis, intense cellular infiltration in the periportal stroma, and fatty metamorphosis of many of the liver cells (figure). Both pathologists who independently reviewed the sections of this tissue (Dr. E. E. Aegerter, Department of Pathology, Temple University School of Medicine, and Dr. B. Lucke, Department of Pathology, School of Medicine, University of Pennsylvania) were inclined to interpret the changes as those of cirrhosis of the Laennec type. Each stated, however, that it was impossible to determine whether the hepatic alterations were results of previous hepatitis.

All available records in the institutions at which the subject admitted having served as a donor were searched, and detailed follow-up data on 18 recipients were obtained. Six of the 18 recipients had died within 40 days after transfusion. Their deaths were due to the various disorders for which transfusion was given. In the 12 who

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Dr. Barondess is a Research Fellow, Communicable Disease Center, U. S. Public Health Service. Dr. Bashe is a Research Fellow, National Institutes of Health, U. S. Public Health Service.

1. Stokes, J. H.; Ruedemann, R., Jr., and Lemon, W. S.: Epidemic Infectious Jaundice and Its Relation to Therapy of Syphilis, Arch. Int. Med. **26**: 521 (Nov.) 1920.

2. Findlay, G. M., and MacCallum, F. O.: Note on Acute Hepatitis and Yellow Fever Immunization, Tr. Roy. Soc. Trop. Med. & Hyg. **31**: 297, 1937; Hepatitis and Jaundice Associated with Immunization Against Certain Virus Diseases, Proc. Roy. Soc. Med. **31**: 799, 1938.

3. Turner, R. H., and others: Some Clinical Studies of Acute Hepatitis Occurring in Soldiers After Inoculation with Yellow Fever Vaccine, with Special Consideration of Severe Attacks, Ann. Int. Med. **20**: 193, 1944.

4. Cockburn, W. C., and others: Homologous Serum Hepatitis and Measles Prophylaxis: Report to Medical Research Council, Brit. M. J. **2**: 6, 1951.

5. Neefe, J. R.; Miller, T. G., and Chornock, F. W.: Homologous Serum Jaundice: Review of Literature and Report of Case, Am. J. M. Sc. **207**: 626, 1944.

survived 40 or more days after transfusion, hepatitis with jaundice developed in 4. One other patient died approximately one year after transfusion and at necropsy was found to have diffuse subacute hepatitis plus atypical periportal cirrhosis. It was impossible, however, to attribute this hepatic damage to the transfusion received one year previously, because the patient had had Hodgkin's disease and multiple hemorrhagic hemangioma of Kaposi (Kaposi's sarcoma) and had been treated with nitrogen mustard at various times during the year preceding death.

None of the four recipients in whom hepatitis with jaundice developed had received plasma, and two had received no blood other than that of the donor under investigation. The pertinent clinical data in these cases were briefly as follows:

Recipient 1, N. C., a 36-year-old woman, was admitted to a local hospital because of hemorrhage accompanying an incomplete abortion. She received only one blood transfusion, 500 cc. from donor W. L., on June 9, 1945. At an unknown and indeterminate time (less than 77 days as fixed by the date on a presumably related prescription blank), jaundice and associated mild gastrointestinal complaints developed. Both of these symptoms persisted for about two weeks but did not require hospitalization.

Recipient 2, W. G., a 40-year-old woman, was admitted to the Albert Einstein Medical Center, Northern Division, because of hypertensive encephalopathy. On Aug. 21, 1947, she underwent the second stage of bilateral thoracolumbar sympathectomy and at this time received a transfusion of 500 cc. of blood from donor W. L. This represented one of six blood transfusions given during this admission. On Sept. 30, 1947, nausea, vomiting, and chilliness occurred and were followed on the next day by malaise, epigastric pain, dark urine, and overt jaundice. Because of these symptoms, the woman was re-admitted to the hospital. Pertinent physical findings consisted of jaundice and a palpably enlarged and tender liver that extended 3 to 4 cm. below the costal margin on deep inspiration.

Recipient 3, C. S., a 41-year-old woman, was admitted to the Albert Einstein Medical Center, Northern Division, because of menorrhagia and dysmenorrhea attributed to uterine fibromyomas. Panhysterectomy was performed on Feb. 12, 1948, on which date the patient received 500 cc. of blood from donor W. L. Previous to this she had received 500 cc. of blood from each of two other donors. On March 10, 1948, nausea, vomiting, and epigastric discomfort developed, and on March 24, 1948, overt jaundice and mild pruritis were noticed. The woman was re-admitted to the hospital where physical findings disclosed jaundice, dehydration, and a barely palpable but tender liver edge.

Recipient 4, B. U., a 50-year-old woman, was admitted to the Albert Einstein Medical Center, Northern Division, with a history of menorrhagia and leukorrhea attributed to uterine fibromyomas. Panhysterectomy was performed on July 20, 1948, on which date the patient received her only transfusion, 500 cc. of blood from donor W. L. Very soon after discharge from the hospital, nausea and vomiting appeared and became intermittent. On Aug. 28, 1948, the urine became darker, and on Sept. 1, 1948, jaundice of the scleras became evident. Physical examination following re-admission to the hospital disclosed jaundice and tenderness in the right upper quadrant of the abdomen, but the liver margin was not palpable.

TABLE 1.—*Data on Liver Function Tests of Donor W. L. in Case 1**

Test	Date 10/12/48	1/19/49	8/9/49	8/23/49	9/12/49
Serum bilirubin					
1 min., mg./100 ml.	0.19	0.06	0.16	0.15	0.09
30 min., mg./100 ml.	0.45	0.49	0.52	0.91	0.63
Cephalin-cholesterol flocculation, 48 hr.	+ 2	Negative	Negative	+ 3	+ 2
Colloidal gold	+ 4	+ 2	+ 3	+ 4	+ 3
Thymol turbidity, units	7.2	3.2	6.2	6.8	6.6
18 hr. turbidity ratio	26%	97%	52%	21%	32%
Gamma globulin, (zinc sulfate) turbidity, units	12.4	9.6	12.5	13.2	12.5
Serum alkaline phosphatase, units †	8.9	5.75	5.91	6.7	7.46
Serum cholesterol					
Total, mg./100 ml.	241	185	270	211	231
Esterified, mg./100 ml.	183	113	163	115	140
% esterized	76%	61%	60%	55%	61%
Serum phospholipid, mg./100 ml.	—	215	268	242	232
Serum fatty acids					
Total, mg./100 ml.	—	274	313	390	283
Cholesterol esterified, fatty acid, mg./100 ml.	—	75	109	77	93
Phospholipid fatty acid, mg./100 ml.	—	143	179	161	155
Neutral fat fatty acid, mg./100 ml.	—	56	25	152	35
Serum neutral fat, mg./100 ml.	—	57	26	160	37
Total serum lipid, mg./100 ml.	—	534	673	690	593
Sulfobromophthalein (Bromsulphalein) retention (2 mg./kg.),30 min.	8.5%	5.0%	4.4%	13.1%	10.9%

* The tests reported in this table were performed in the laboratories of the Fels Research Institute of Temple University School of Medicine under the supervision of Dr. Harry Shay.
† Shinowara-Jones-Reinhart.

The period from receipt of blood to onset of overt jaundice was 41, 41, and 43 days, respectively, in the three recipients about whom accurate information could be obtained. All four patients made uneventful recoveries.

In view of these findings pointing to W. L. as a carrier of hepatitis virus, an attempt was made to improve his hepatic situation and, at the same time, perhaps to nullify the apparent infectiousness of his blood by a prolonged course of therapy with chlortetracycline (Aureomycin). Accordingly, on Aug. 10, 1949, he was given chlortetracycline in a dose of 250 mg. four times daily. This dosage was increased on Aug. 19 to 500 mg. four times daily and maintained at this level until Sept. 10. Liver function tests made just before, during, and immediately after the therapy with chlortetracycline failed to disclose any significant improvement in hepatic function (table 1). Similarly, hepatic tissue, obtained by aspiration biopsy

on Sept. 12, 1949, immediately after completion of the course of chlortetracycline, showed no change in the degree of periportal fibrosis and periportal cellular infiltration. It was noted, however, that the liver cells showed definite fatty change that appeared to be more diffuse than in the previous biopsy sample. The latter is of interest in light of the observations since made on fatty changes in the liver and abnormalities in liver function after the administration of chlortetracycline and oxytetracycline (Terramycin).[6]

We tried also to discourage the subject from serving as a blood donor in the future. Local agencies dealing with professional blood donors were warned about using his blood. Despite these precautions, on at least two other occasions of which we are aware he succeeded in having his blood accepted at local hospitals, once by changing his name. Fortunately, the blood was apprehended both times before it could be used. He was also prevented from an attempted donation of blood in another city under his own name. It is entirely likely, however, that other donations were made by him without our knowledge, and these probably were accepted and used.

TABLE 2.—*Results of Inoculation of Serum from Donor W. L. into Volunteers*

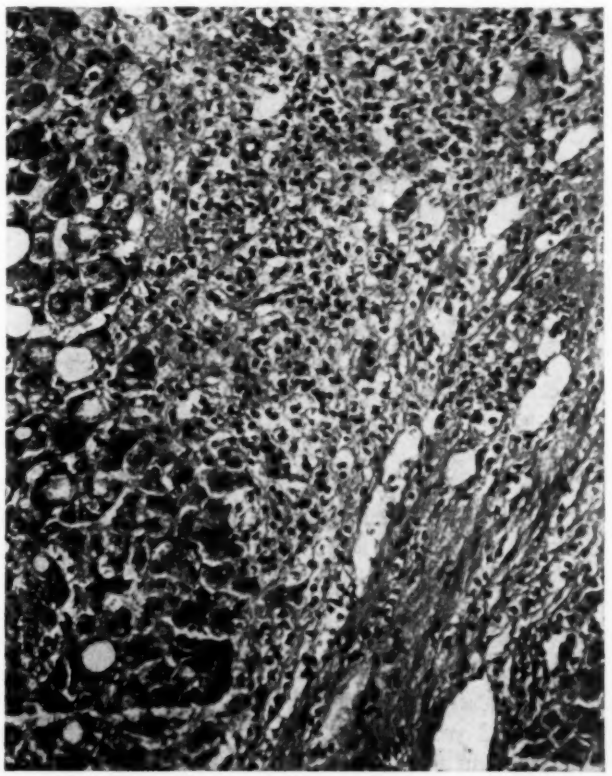
Volunteer	Clinical Evidence	Laboratory Evidence	Interval Between Inoculation and Jaundice or Other Evidence	Interpretation	
				Hepatitis	Jaundice
J. F.	+	+	68	+	+
R. S.	±	0	33	?	—
O. M.	0	0	—	—	—
H. M.	0	0	—	—	—

Observations in Volunteers.—For tests in volunteers, serum was obtained from donor W. L. on Nov. 15, 1950, and stored at −10 C. This was approximately five and one-half years after the date of administration of his blood to the first recipient in whom hepatitis with jaundice was known to have developed. Four male volunteers, R. S., O. M., J. F., and H. M., were carefully screened by the usual liver function tests and physical examinations, and each was injected intramuscularly on April 5, 1951, with 2 ml. of W. L.'s serum. The usual follow-up [7] of liver function tests obtained at regular weekly intervals and physical examinations were conducted on all volunteers. The results are recorded in table 2. Although jaundice did not appear in J. F. until the 68th day, clinical symptoms began on the 33rd day, and mildly positive liver function tests followed immediately on the 34th day. These increased intermittently up to the time of appearance of jaundice. During the same period, R. S. had mild symptoms involving the right upper quadrant of the abdomen, but his liver function tests were normal. Consequently, he must be considered to have had a questionable case of hepatitis, without jaundice.

In addition, eight female volunteers were similarly screened by the usual liver function tests and physical examinations, and each received orally a preparation of W. L.'s stools. The usual follow-up of liver function tests [7] obtained at weekly intervals and physical examinations were conducted on all volunteers. No hepatitis occurred.

Clinical Observations in Case 2.—The infant son of this patient, Mrs. G. A., has been reported on quite briefly previously [8] and will be discussed more fully elsewhere. It is sufficient here to indicate that this infant was selected for study out of the increasing number of newborn infants in whom it has been suspected that viral hepatitis with jaundice developed soon after birth. In this case, infection through the birth canal could be ruled out, since the baby was delivered by cesarean section. Transmission by means of breast milk could be eliminated, because the baby was not breast fed and was separated from its mother. When jaundice developed in the child at the age of 2 months, it was suggested that transplacental transmission of serum hepatitis might have occurred, although the mother had no history of liver disease.

Observations in Volunteers.—In view of the development of chronic hepatitis with jaundice in the infant at two months, blood was obtained from the infant and the mother during this period, i. e., at nine months, for use



Photomicrograph of liver tissue obtained by aspiration biopsy in W. L. (donor in case 1) showing periportal fibrosis, periportal cellular infiltration, and fatty metamorphosis.

in volunteers. The serums of the infant and the mother were each injected parenterally into five volunteers. The results of these injections, together with the incubation periods of the resulting hepatitis are shown in table 3. Although overt jaundice was absent in the three cases of hepatitis in the volunteer recipients of the mother's blood, it is of particular interest that volunteer Ma had a

6. Lepper, M. H., and others: Effect of Large Doses of Aureomycin on Human Liver, A. M. A. Arch. Int. Med. **88**: 271 (Sept.) 1951. Lepper, M. H., and others: Effect of Large Doses of Aureomycin, Terramycin, and Chloramphenicol on Livers of Mice and Dogs, ibid. **88**: 284 (Sept.) 1951. Rutenberg, A. M., and Pinkes, S.: The Hepatotoxicity of Intravenous Aureomycin, New England J. Med. **247**: 797, 1952.

7. Drake, M. E., and others: Studies on Agent of Infectious Hepatitis: II. Disease Produced in Human Volunteers by Agent Cultivated in Tissue Culture or Embryonated Hens' Eggs, J. Exper. Med. **92**: 283, 1950.

8. Stokes, J., Jr., and others: Viral Hepatitis in the Newborn: Clinical Features, Epidemiology and Pathology, Am. J. Dis. Child. **82**: 213 (Aug.) 1951.

slightly higher serum bilirubin level than volunteer Ha, who had overt jaundice after receiving the infant's blood. Such a paradoxical relation between jaundice and serum bilirubin is a well-recognized phenomenon that is occasionally encountered. The incubation periods were in the range usually recorded for serum hepatitis. The clinical course in all five volunteers was marked by nausea and occasional vomiting, marked tenderness in the right upper quadrant of the abdomen with enlargement of the liver, occasional diarrhea, and at least two, or sometimes three or more, positive liver function tests, including elevations of serum bilirubin in two of the volunteers, as previously mentioned.

The results of the mother's liver function tests—serum bilirubin, sulfobromophthalein (Bromsulphalein) retention, cephalin-cholesterol flocculation, thymol turbidity and flocculation, and alkaline phosphatase—were well within the normal range. In the infant, however, as recorded elsewhere, a liver biopsy indicated marked

TABLE 3.—*Results of Inoculation of Serum from Mrs. G. A. and the Serum of Her Infant into Volunteers*

Volunteer	Clinical Evidence	Laboratory Evidence	Interval Between Inoculation and Jaundice or Other Evidence	Interpretation: Hepatitis	Interpretation: Jaundice
Infant's serum					
Ha	+	+	100	+	+
Ap	0	+	75	+	0
Cl	0	0	—	0	0
Hab	0	0	—	0	0
We	0	0	—	0	0
Mother's serum					
Ma	+	+	91	+	0
Tk	+	+	90	+	0
Si	0	+	89	+	0
Sc	0	0	—	0	0
Wes	0	0	—	0	0

fibrosis of the liver, and the child later died at the age of 18 months with advanced fibrosis of the liver. After a period of 2 years and 11 months from the date of the infant's birth, a second sample of the mother's blood was drawn for the purpose of determining whether she continued to be a "silent carrier" of hepatitis virus B. She also requested information, however guarded and incomplete it might be, concerning whether, in a contemplated pregnancy, her infant again might be subject to serum hepatitis. On Jan. 1, 1951, each of five volunteers (table 4), was injected with 2 cc. of the mother's serum. After the usual long incubation periods, as shown in the table, two cases of hepatitis with jaundice and one case of hepatitis without jaundice occurred in the volunteers. This result added considerable weight to the earlier observations, in which three of five other volunteers had had hepatitis without jaundice when injected with the mother's serum.

Clinical Observations in Case 3.—In September, 1950, Mrs. E. W. became sick 50 days after receiving seven transfusions of packed red blood cells. Eight days later jaundice developed and a diagnosis of homologous serum jaundice (viral hepatitis B) was made. The patient recovered.

In January, 1951, a patient, Mrs. L. B., died of hepatic necrosis 73 days after transfusion with four bottles of dried plasma and two bottles of preserved blood. Her first complaint was of jaundice 53 days after transfusion. Investigation of the donors who had contributed the blood and the plasma did not reveal anything of obvious significance. It was noticed, however, that the blood of one of these donors (P. J. G.) had been given to Mrs. E. W. and that his blood had also been used in the preparation in January, 1950, of a nine donor pool of plasma, G. 997, from which four 400 ml. bottles of plasma were dried. One of these had been given to Mrs. L. B.

TABLE 4.—*Results of Inoculation of Second Sample of Serum from Mrs. G. A. into Volunteers*

Volunteer	Clinical Evidence	Laboratory Evidence	Interval Between Inoculation and Jaundice or Other Evidence	Interpretation: Hepatitis	Interpretation: Jaundice
F. O.	+	+	67	+	+
V. G.	+	+	76	+	+
A. P.	0	+	71	+	0
L. P.	0	0	—	0	0
J. H.	0	0	—	0	0

In April, 1951, a third patient, Mrs. H. J., became sick 54 days after transfusion with three bottles of blood and one bottle of dried plasma. Jaundice developed 15 days later, and homologous serum jaundice was diagnosed. The patient recovered. On investigation it was found that the bottle of plasma was from batch G. 997 that had also been given to Mrs. L. B.

The donor, P. J. G., was now associated with three cases of homologous serum jaundice. He was again visited. He was 39 years old and worked in a cement factory. He was in good health and active. There was no history of any illness or absence from work since his discharge from the Army in 1946. He had been a prisoner of war in Siam and had had malaria; the last attack occurred in 1945. Apart from an occasional attack of diarrhea, he had had no other illness as a prisoner. There was nothing in his medical history to suggest that he had ever had hepatitis. Physical examination revealed no abnormalities. The liver was not palpable. A sample of blood was collected, and the following report of the tests was made:

Van den Bergh	
Direct	Negative
Indirect	Serum bilirubin, 0.9 mg. per 100 cc.
Thymol turbidity	15.5 units
Gamma globulin ($ZnSO_4$ turbidity)	30 units (2.2 gm. per 100 cc.)
Total serum protein	6.8 gm. per 100 cc.
Serum albumin	4.6 gm. per 100 cc.
Albumin/globulin ratio	2.1/1
Alkaline phosphatase	13 King-Armstrong units

It now seemed highly probable that P. J. G. was a carrier of the virus of homologous serum jaundice and that transfusion of his blood, or plasma made from his blood, was responsible for the transmission of homologous serum jaundice to Mrs. E. W., Mrs. L. B., and Mrs. H. J. His name was removed from the blood donor panel.

Observations in Volunteers. — Approximately 10 months after the date of the first infected recipient's transfusion with P. J. G.'s blood, a specimen of his (P. J. G.'s) blood was drawn, and the serum was brought to the United States—frozen in dry ice—by Dr. Zeitlin. This serum was injected, 2 cc. parenterally, into each of five volunteers. In one hepatitis with jaundice developed 59 days after injection (table 5). The evidence was clear-cut that the blood of P. J. G. carried virus SH (viral hepatitis B) over a period of at least 10 months.

VIRAL HEPATITIS A

In this disease, man is the only animal that can readily be used for determining the carrier state. In contrast to viral hepatitis B, in which the virus apparently is present in the blood but not in the stools, the virus in viral hepatitis A (IH) may be found in large quantities in the stools, as well as in the blood. Thus, carriers conceivably could have virus in both stools and blood. In general, the short incubation periods that characterize viral hepatitis A have been rare in hepatitis resulting from injection of pooled plasma or in hepatitis caused by single transfusions. In experimental detection of virus in viral hepatitis A (IH) by inoculation of volunteers, viremia was found for only a relatively short period preceding and during the acute stage of the disease. The duration of fecal excretion of the virus appears to be relatively short in most cases, although a fecal carrier state has been postulated by some to explain some aspects of the epidemiology of the disease.

The two children reported here as fecal carriers, or as having chronic active hepatitis without jaundice, aided in completing the picture of endemic hepatitis in a Chicago orphanage previously reported.[9] Their courses are more fully outlined here, and deservedly so, since to our knowledge they represent the first proved carriers of viral hepatitis virus A.

TABLE 5.—*Results of Inoculation of Serum from Donor P. J. G. (Case 3) into Volunteers*

Volunteer	Clinical Evidence	Laboratory Evidence	Interval Between Inoculation and Jaundice or Other Evidence	Interpretation	
				Hepatitis	Jaundice
C. R.	+	+	59	+	+
S. S.	0	0	—	0	0
J. S.	0	0	—	0	0
W. S.	0	0	—	0	0
A. V.	0	0	—	0	0

Clinical Observations in Case 4.—This 28-month-old white girl, G. A., was apparently well until Aug. 21, 1949, when frequent loose stools occurred. On Aug. 24, 1949, a low grade fever appeared and was associated with anorexia, lethargy, and abdominal distension. On Aug. 31, 1949, the liver edge was palpable 4 fingerbreadths below the right costal margin. Laboratory tests were first performed on Sept. 1, 1949, at which time marked abnormalities were found in the ammonium sulfate turbidity, thymol turbidity, thymol flocculation, and scarlet red tests. Subsequently, the cephalin-cholesterol flocculation, serum alkaline phosphatase, and serum cholinesterase were found to be abnormal.

Rather marked symptoms continued until December, 1949, and then were intermittent for one year. The liver decreased in size after seven weeks to 2 fingerbreadths below the costal margin, where it remained for six months. Abnormal laboratory findings decreased somewhat by January, 1950, but continued intermittent through December, 1950.

Observations in Volunteers.—Feces obtained on Jan. 27, 1950, were tested by administering 2 cc. of a 20% saline suspension of stool orally to each of four volunteers. After an incubation period of 22 days, hepatitis with jaundice developed in one of the volunteers, G. M., as recorded in table 6.

Clinical Observations in Case 5.—In this 11-month-old girl, M. C., unexplained fever developed on Dec. 5, 1949, and lasted eight days. On Dec. 12, failure to gain weight was noted, and on Dec. 18 there were light-colored loose stools and moderate lassitude. On Jan. 9, 1950, the liver was palpable 2½ fingerbreadths below the right costal margin. Marked abnormalities were found at this time in the ammonium sulfate turbidity, thymol turbidity, thymol flocculation, scarlet red, and serum alkaline phosphatase tests of liver function.

Recurrent loose stools, fever, and lassitude continued until September, 1951. Liver function tests were much improved in February, 1950, but became markedly abnormal in April, 1950, and continued so, with occasional short remissions, until September, 1951. Late in March, 1950, the serum cholinesterase level and cephalin flocculation were also markedly abnormal.

TABLE 6.—*Results of Oral Inoculation of Preparation of Stool from G. A. (Case 4) in Volunteers*

Volunteer	Clinical Evidence	Laboratory Evidence	Interval Between Inoculation and Jaundice or Other Evidence	Interpretation	
				Hepatitis	Jaundice
G. M.	+	+	22	+	+
C. M.	0	0	—	0	0
C. C.	0	0	—	0	0
A. M.	0	0	—	0	0

Observations in Volunteers.—Feces obtained from this infant on March 15, 1951, were tested by administering 2 cc. of a 20% stool suspension orally to each of four volunteers. After an incubation period of 26 days, as recorded in table 7, hepatitis with jaundice developed in one of the volunteers.

COMMENT

It deserves emphasis that the weight of the evidence reported here for carriers of hepatitis virus B (SH) lies not only in the production of hepatitis with jaundice in a few volunteers but on the combined weight of epidemiological evidence from jaundice in recipients of the blood of carriers plus the direct evidence in volunteers. It is well, however, to clarify the value of the occurrence of hepatitis with jaundice in one out of a group of four or five volunteers, since a number of the conclusions as to carriers in the present report must depend for direct evidence on such a single occurrence. The value of such a single case, with jaundice, would appear to be significant for the following reasons. No volunteer was accepted

TABLE 7.—*Results of Oral Inoculation of Preparation of Stools from M. C. (Case 5) in Volunteers*

Volunteer	Clinical Evidence	Laboratory Evidence	Interval Between Inoculation and Jaundice or Other Evidence	Interpretation	
				Hepatitis	Jaundice
J. K.	+	+	26	+	+
R. K.	0	0	—	0	0
W. M.	0	0	—	0	0
L. H.	0	0	—	0	0

9. Capps, R. B.; Bennett, A. M., and Stokes, J., Jr.: Endemic Infectious Hepatitis in an Infants' Orphanage: I. Epidemiologic Studies in Student Nurses, A. M. A. Arch. Int. Med. **89**: 6 (Jan.) 1952. Bennett, A. M., and others: Endemic Infectious Hepatitis in an Infants' Orphanage: II. Epidemiologic Studies in Infants and Small Children, ibid. **90**: 37 (July) 1952.

for the studies unless he had been isolated in prison for a long period and unless he had been carefully examined both by physical examination and by liver function tests. Also, inoculations were not made and were not considered as valid evidence, if hepatitis occurred in the uninoculated prisoners in the institution, either before or after the studies. Thus, to consider the occurrence of jaundice in a volunteer prisoner at exactly the right incubation period after inoculation as a chance infection would be similar to considering mumps in a child exposed at home to a sibling with mumps as a chance infection, when there have been no other cases of mumps in the area and the disease develops in the second sibling at precisely the right period after exposure to the first child.

Statistically, one must consider all the days of a prisoner's life, except perhaps those of the first nine months, as being days on which he might have had jaundice. That jaundice developed at exactly the time that accorded with the end of a proper incubation period, as calculated from the day of his inoculation, provides strong evidence for the validity of the conclusion that the inoculum he received was the source of the infection. Such a conclusion would not be valid under ordinary circumstances of civilian life, as, for example, when a hospitalized patient receives a single transfusion and serum hepatitis with jaundice develops 60 to 90 days later. Such hospital patients are always subjected to injections for various reasons and may be exposed by chance to persons with incipient or active epidemic hepatitis, while such opportunities for infection can be virtually eliminated in prisons under the precautions taken for volunteers. Even in such hospital patients, jaundice at the end of the correct incubation period following such a single transfusion would result in strong suspicion concerning the infectivity of the donor's blood, but obviously there would not be such conclusive evidence as is afforded by prison isolation and volunteer inoculation. It is difficult to believe that cases of jaundice would occur regularly in the several groups of inoculated volunteers in the prison and in no other prisoners unless the inoculations were solely responsible for the jaundice. For all of the above reasons, the circumstantial evidence in the clinical histories added to the direct evidence obtained in volunteers appears to be conclusive.

In addition, the single cases of hepatitis with jaundice in each of the two groups of four volunteers who received orally the stool preparations from the carriers of IH virus in the Chicago orphanage afford clear-cut positive evidence in that both volunteers had characteristically short incubation periods and were well selected and well isolated in prison. Thus, there could be no reason to believe that by chance alone epidemic hepatitis with jaundice would have developed in both at the end of the expected incubation period.

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10. Deleted on proof.

11. Best, C. H.; Hartroft, W. S.; Lucas, C. C., and Ridout, J. H.: Liver Damage Produced by Feeding Alcohol or Sugar and Its Prevention by Choline, Brit. M. J. **2**: 1001, 1949.

12. Havens, W. P., Jr.: Serum Hepatitis in Viral and Rickettsial Infections of Man, ed. 2, Rivers, T. M., editor, Philadelphia, J. B. Lippincott Company, 1952.

One of the most interesting findings in the present studies is the absence of a history of jaundice in any of these carriers of hepatitis virus B. This noncontributory history also obtained in the persons is described in the companion reports by Neefe and others and Murray and associates that follow. Even though all of the carriers described in both reports were discovered in retrospect, i. e., from the histories of those whom they infected, this lack of history of jaundice in the carriers may be important. The possibility exists that such carriers are persons who have not suffered sharp attacks of hepatitis, with the development of solid immunity, but rather those in whom only partial immunity develops and in whom the infection continues to smolder for long periods. It should be borne in mind, however, that blood donors are a selected group in that those with a history of jaundice are not accepted; hence, it may be expected that carriers identified through the development of hepatitis in recipients of their blood will, in general, not give a history of jaundice. The biopsy appearance of W. L.'s liver and the livers of carriers described in the paper that follows may indicate liver injury from another source, and yet may also indicate a continuing activity of the hepatitis viruses that is being carried in the blood and that may also continue to be active in the liver. It is conceivable that, in the case of W. L., the effect of alcohol in increasing metabolic activity of the liver cells may have also increased the susceptibility of these cells to the hepatitis virus. Best and associates [11] have demonstrated that, in mice eating diets deficient in choline to a degree just short of producing cirrhosis, cirrhosis will develop quite readily if small amounts of alcohol are added to the diet, with resultant increase of metabolic activity.

It may be significant that the three infected recipients of W. L.'s blood had incubation periods of 41, 41, and 43 days that are short for the usual case of serum hepatitis, while the incubation periods in the volunteer injected with W. L.'s blood was longer, i. e., 68 days. Since signs of hepatitis often appear throughout the incubation period of serum hepatitis, it is conceivable that in an already damaged liver the onset of the fullblown disease might well be accelerated. It is also conceivable that viral hepatitis A (IH) might have been responsible or even that W. L. might have been a carrier of more than one antigenic strain of virus and that the volunteer who had hepatitis with jaundice might have been resistant to hepatitis A; this would have permitted the disease of longer incubation (hepatitis B) to occur. The apparent absence of virus in W. L.'s stool, at least at the time it was tested orally in volunteers, also somewhat favors his classification as a carrier of hepatitis virus B (SH). The absence of serologic tests for such differentiation makes such considerations highly speculative at best.

Havens [12] has reported on a presumptive carrier in whom identification of the carrier state was based on the circumstantial evidence that hepatitis with jaundice developed in two recipients four months after they received his blood and that jaundice developed in the donor himself one year after his blood was last used. It is entirely possible that the jaundice in this case was from another

virus source, since, as has been suggested,[13] persons infected with hepatitis virus B (SH) may thereby become actually more susceptible to epidemic hepatitis.

Ginzburg and associates [14] described two donors whose blood apparently caused hepatitis with jaundice in three and two recipients, respectively. These donors had no history of jaundice and did not ever have jaundice later on. Their blood was not studied in volunteers, but later liver function tests (thymol turbidity and cephalin flocculation) showed marked abnormalities in both donors.

Mrs. G. W. (case 2) of the present report is unique in that she appears to have been a "silent carrier" for at least three years. (The term "silent carrier" is used to indicate a carrier who has neither symptoms nor positive liver function tests.) The apparent occurrence of transplacental transmission to her infant may help to explain some aspects of the epidemiology of viral hepatitis B. If large numbers of "silent carriers" exist, and there are many reasons to believe they do, such transmission from the mother, or even by semen from one generation to the next, may account for some of these carriers. This possibility deserves further investigation.

The presence of carriers among professional blood donors, who depend to an extent for their living and, as in W. L.'s case, at times for their alcohol on the donor fees, and the absence of a history of jaundice (the main criterion being used by many groups for screening of donors) add greatly to the seriousness of the problem and to the difficulty of its control. Ultraviolet irradiation by the apparatus now in use is not as yet consistently effective in the elimination of hepatitis virus B (SH) from plasma and serum, and no method has yet been used successfully to disinfect whole blood. While no accurate method has been found for the detection of carriers, the present studies on the patients in our cases 1 and 3, those reported by Ginzburg and associates,[14] and in particular those mentioned in the following paper suggest that the exclusion from blood donor panels of certain persons with positive liver function tests might reduce the incidence of hepatitis B.

Two previous studies have been made on single volunteers convalescent from viral hepatitis B (SH) with jaundice to determine whether the virus remained in the blood over long periods of time. In these preliminary experiments, no evidence was obtained that the virus remained in the blood. Such studies require further extension.

The finding of fecal carriers of hepatitis virus A (epidemic hepatitis [IH] virus) also was not unexpected. Many outbreaks of this disease and its endemic characteristics in certain areas would be difficult to explain if human carriers or chronic active states did not exist. These children were not "silent carriers" since their liver function tests were mildly positive over a considerable period of time. The chronic nature of their symptoms, the endemic nature of the disease in the orphanage, and the continuously positive liver function tests strongly suggest that the virus was continuously present for a long period in their stools.

SUMMARY AND CONCLUSIONS

The detection, by circumstantial evidence and by direct evidence in volunteers, of three persons who carried hepatitis virus B in their blood and of two who carried hepatitis virus A in the feces is described. The blood-borne viruses appear to have been present for at least five and one-half, three, and one year in the respective hepatitis virus B carriers, while the hepatitis virus A was present in the stools for indeterminate periods.

The lack of history of jaundice and the absence of symptoms in the three carriers of hepatitis virus B are emphasized. However, positive liver function tests were present in the patients in cases 1 and 3, and a markedly damaged liver was evident in a biopsy section from the patient in case 1. The patient in case 2 apparently was a "silent carrier" for at least three years and, at the same time, had neither symptoms nor abnormal liver function tests. Some aspects of the epidemiology of viral hepatitis B may be partially explained by what appeared to be transplacental transmission of the virus in case 2. The two fecal carriers of hepatitis virus A had symptoms, but no jaundice, and mildly positive liver function tests. It is suggested that the development of the carrier state may occur when the host fails to attain a solid immunity early in the course of infection with one of these viruses.

Improved methods for the control of viral hepatitis B must await the development of efficient techniques for eliminating or inactivating hepatitis virus B in whole blood or blood products or techniques for easy and rapid identification of carriers. Until such techniques are available, elimination of donors with histories of jaundice and/or abnormal liver function tests may help in reducing the incidence of the disease.

1740 Bainbridge St. (46) (Dr. Stokes).

13. Gauld, R. L.: Epidemiological Field Studies of Infectious Hepatitis in Mediterranean Theater of Operations: Clinical Syndrome, Morbidity, Mortality, Seasonal Incidence, Am. J. Hyg. 43: 248, 1946.

14. Ginzburg, L.; Sussman, L. N., and Auerhan, H.: Posttransfusion Viral Hepatitis as Surgical Complication, Surg., Gynec. & Obst. 92: 492, 1951.

Histoplasmosis.—Studies in Ohio have shown that within the state there is a definite pattern for proved cases of histoplasmosis that coincides with the distribution of histoplasmin reactors and pulmonary calcifications. This demonstrated correlation of skin test, pulmonary calcifications and proved cases suggests that the histoplasmin skin test, even though it may have cross reactions with other fungi, is usually indicative of past or present, clinical or subclinical infection with *Histoplasma capsulatum*. Studies of clinical histoplasmosis reveal that there tends to be a greater incidence of the disease in the extremes of life. Although the sex distribution is approximately equal among infants and children, the male is more frequently involved after 10 years of age. Accumulated data confirm the growing concept that histoplasmosis is not universally fatal. In fact, the increasing number of cases, reported and unreported, in which the patients recover suggests that it may well be a common infection with relatively few fatalities Histoplasmosis is characterized by protean manifestations. They may include irregular fever, weight loss, cachexia, anorexia, nausea, "indigestion," vomiting, diarrhea, jaundice, cutaneous or mucosal ulcerations, cough, sputum, pneumonia that is refractory to all antibiotics, hepatomegaly that occasionally is accompanied by jaundice, splenomegaly and lymphadenopathy. Leukopenia and anemia are common in the more advanced disease. The course may vary from a mild vague illness lasting a few days or weeks to a very fulminating, rapidly fatal disease. Thus, in the usual absence of pathognomonic signs and symptoms, the detection of histoplasmosis requires, first, a high index of suspicion, and second, a specific program of clinical and laboratory study.—J. A. Prior, M.D.; Saslaw, M.D., Ph.D., and C. R. Cole, D.V.M., Experiences with Histoplasmosis, *Annals of Internal Medicine*, February, 1954.

CARRIERS OF HEPATITIS VIRUS IN THE BLOOD AND VIRAL HEPATITIS IN WHOLE BLOOD RECIPIENTS

1. STUDIES ON DONORS SUSPECTED AS CARRIERS OF HEPATITIS VIRUS AND AS SOURCES OF POST-TRANSFUSION VIRAL HEPATITIS

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In spite of intensive efforts to develop methods for the detection or inactivation of hepatitis virus in human whole blood and plasma, none has been satisfactorily proved to be uniformly effective to date.[1] The clinical use of these indispensable therapeutic agents, particularly whole blood and plasma used for transfusion, continues to be associated with an ever-present risk of the serious complication of viral hepatitis. Until practical and dependable methods for detection or inactivation of hepatitis virus in blood and plasma become available, physicians are obligated to reserve their use of these materials for clinical conditions in which their potential value outweighs the risk of the potential complication of viral hepatitis, a decision that is not always easy to make. In recent years, while awaiting the development of such methods, an effort has been made to decrease the frequency of collection of blood contaminated with hepatitis virus by rejection of donors who have been exposed to hepatitis or who have had hepatitis or jaundice.[2] In spite of this precaution, the best available information indicates a minimal incidence of viral hepatitis between 0.45 and 1% following the use of whole blood alone for transfusion. The incidence following the use of pooled plasma depends on the number of plasma units included in a pool and apparently may range from 1 to 20%.[3]

It is apparent, therefore, that the continued serious incidence of post-transfusion viral hepatitis must be due mainly to the existence of a large reservoir of asymptomatic, apparently healthy blood carriers of hepatitis virus who either have not had or do not admit previous recognized hepatitis or jaundice. Strong circumstantial evidence of such a carrier state has been provided by Berk and Malamut in their recognition of a donor who gave blood, at different times over a period of five and one-half years, to various recipients in whom post-transfusion hepatitis developed.[4] Clinical study of this donor revealed physical, laboratory (hepatic function tests), and biopsy evidence of chronic liver disease compatible with cirrhosis.

For some time, we have been interested in the possibility that some such carriers might present subclinical abnormalities, detectable by hepatic function screening tests, that would lead to recognition of them as potential carriers.[4a] Since 1950, we have studied carefully the 22 persons who donated blood for 14 patients in whom viral hepatitis developed after transfusion of one (8 patients), two (4 patients), or three (2 patients) units of whole blood. Results of certain hepatic function tests were abnormal in an unexpectedly high proportion of the suspected donors, all of whom had met the standard criteria for acceptance as a blood donor.[2] The details of this study are presented in this report. The second part of this paper presents data, obtained by means of transmission studies in volunteers, that appear to establish with certainty the existence of a blood carrier state in five of the six suspected donors so tested. Some of these data have been presented in abstract form elsewhere.[5]

SCOPE OF STUDY

The 14 patients with apparent post-transfusion viral hepatitis had received transfusions of only whole blood. The time interval between the transfusion and the onset of hepatitis in each recipient was compatible with the incubation period of viral hepatitis caused by either the so-called infectious hepatitis (IH or A) or the serum hepatitis (SH or B) type of virus.[4a] The diagnosis of viral hepatitis in each recipient was based on careful clinical evaluation of the underlying disease that occasioned transfusion together with the course and characteristics of the attack of transitory jaundice. One recipient died of massive necrosis of the liver. Eight of the recipients received only a single transfusion; four received transfusions from two donors; and two received transfusions from three donors.

The 22 donors were studied after suspicion of their potentially infectious state had been aroused by the occurrence of hepatitis in the recipients. Except for donors 12a and 12b, none had had hepatic function tests at the time of the original donation. The interval between the

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Miss Virginia Yonan, Miss Anne Mifflin, Mrs. Helen Hall, Mrs. Jane Bender, and Dr. Neva Abelson assisted in the tracing and study of the blood donors.

1. Murray, R., and others: To be published.

2. Minimum Requirements: Citrated Whole Blood (Human), 3rd Revision, National Institutes of Health, Public Health Service, Bethesda, Md., Feb. 19, 1953.

3. Spurling, N.; Shone, J., and Vaughan, J.: Incidence, Incubation Period, and Symptomatology of Homologous Serum Jaundice, Brit. M. J. **2**: 409 (Sept. 21) 1946. Brightman, I. J., and Korns, R. F.: Homologous Serum Jaundice in Recipients of Pooled Plasma, J. A. M. A. **135**: 268 (Oct. 4) 1947. MacCallum, F. O.: Recent Advances in Infective Hepatitis and Serum Hepatitis, Proc. Fourth Internat. Cong. Trop. Med. & Malaria **1**: 457 (May 10-18) 1948. Sborov, V. M.; Giges, B., and Mann, J. D.: The Incidence of Hepatitis Following the Use of Pooled Plasma, Arch. Int. Med. **92**: 678 (Nov.) 1953. Allen, J. G., and others: Homologous Serum Jaundice and Its Relation to Methods of Plasma Storage, J. A. M. A. **144**: 1069 (Nov. 25) 1950.

4. (*a*) Neefe, J. R.: Viral Hepatitis: Problems and Progress, Ann. Int. Med. **31**: 857 (Nov.) 1949. (*b*) Berk, J. E., and Malamut, L. L., quoted by Neefe.[4a]

5. Neefe, J. R., and others: Demonstration of the Existence of Asymptomatic Blood Carriers of Hepatitis Virus: Relationship of Carriers to Acute Viral Hepatitis in Whole Blood Recipients; Proceedings of the 44th Annual Meeting of American Society for Clinical Investigation, J. Clin. Invest. **31**: 652 (June) 1952.

time of donation and the time of reevaluation varied between 43 and 294 days. Detailed histories were obtained, and thorough physical examinations were made. Specimens of blood and urine were collected for the hepatic function tests shown in table 1. Tests for the presence of urine bilirubin, which were uniformly negative, are not included in the table. When available additional blood serum for future use was also stored at −15 to −20 C.

TABLE 1.—*Hepatic Function Tests Used as Criteria for Classification as Normal, Equivocal, and Abnormal**

Test	Mean ± 2 S.D.† Normal	Mean + 2-3 S.D.† Equivocal	Method
Total serum bilirubin, mg./100 ml.	1.10	1.10-1.35	Malloy and Evelyn
1 minute bilirubin, mg./100 ml.	0.21	0.21-0.27	Ducci and Watson
Thymol turbidity (pH 7.8), units	4.4	4.4-5.5	Maclagan; Shank and Hoagland; and Neefe et al.
Thymol flocculation (pH 7.8)	0, ±	1+	
Thymol turbidity (pH 7.55), units	5.5	5.5-6.6	Mateer et al.; Shank and Hoagland; and Neefe et al.
Thymol flocculation (pH 7.55)	0, ±	1+	
Cephalin flocculation (24 hr.)	0	±	Hanger; and Neefe and Reinhold
Cephalin flocculation (48 hr.)	0, ±, 1+	2+	
Zinc turbidity, units	9.6	9.6-12.5	Kunkel et al.
Urine urobilinogen (random), Ehrlich units	1.15	1.15-1.47	Watson et al.
Sulfobromophthalein retention, %	7.0	7.0-8.7	Reinhold and Hutchinson

* Results exceeding the upper limit of the equivocal range are regarded as abnormal or positive.
† Standard deviation.

The values shown for the normal and equivocal ranges of the tests employed are those obtained from an earlier study [6] of presumably normal young adults. Values exceeding the mean by more than three standard deviations (not shown in table) were considered abnormal. For the sake of brevity, the results that exceed the normal range are called either equivocal (mean ± 2 to 3 S. D.) or positive (exceeding the mean ± 3 S. D.). The sulfobromophthalein sodium retention test was performed by injection of 5 mg. of dye per kilogram of ideal body weight, with photoelectric measurement of retention after 45 minutes.

Brief data for each of the 14 recipients are presented in table 2. Data, including the results of hepatic function tests, on the 22 donors are given in table 3, and the relation of the donors to each of the 14 recipients is indicated. Brief case reports on six of the original recipients and on their six respective donors, whose serum subsequently was tested for infectivity in human volunteers, are presented as all but one (donor 1) of these donors eventually were proved to be blood carriers of hepatitis virus. Although the carrier state was not proved by volunteer studies, the history of donor 12a, suspected as the source of infection in recipient 12, also is included in the text because a liver biopsy was obtained from this donor.

REPORT OF CASES

RECIPIENT 1.—F. M., a 66-year-old woman, was operated on on June 26, 1950, for multiple polyps of the transverse colon. Transverse colectomy and cecostomy were performed. During the operation, she received one unit of 500 ml. of blood. Postoperative convalescence was uneventful, but, on Aug. 30, 65 days after transfusion, she began to have upper abdominal pain and 2 days later she became jaundiced. For the three weeks following, she had nausea, indigestion, and subcostal pain on the right side and passed dark urine and light stools. Early in October, jaundice and most of the symptoms disappeared and she felt relatively well. Hepatic function tests on Sept. 12 were compatible with parenchymatous hepatic disease. Sulfobromophthalein sodium retention on Oct. 9, 1950, was 20% and on Nov. 25 6.4%.

DONOR 1.—W. C., a 28-year-old man, when reexamined on Oct. 6, 1950, 111 days after donation of blood, denied previous illness. He would not come to the hospital for a sulfobromophthalein sodium retention test or for liver biopsy, but specimens of blood were obtained from him on three occasions. The results of hepatic function tests are shown in table 3. The zinc turbidity was positive, and the thymol turbidity at pH 7.55 was equivocal. Results of these tests remained abnormal on subsequent examination on Jan. 5, 1951, and on June 11, 1952, one year and 261 days after the original donation.

RECIPIENT 2.—L. G., a 40-year-old woman, was operated on on July 19, 1950, for carcinoma of the breast. At that time she received 500 ml. of blood. In August and early September, she received roentgen ray therapy for regional metastases. Nausea and vomiting began in September, 48 days after transfusion, and 3 days later jaundice appeared together with excretion of dark urine and light stools. Elevated total serum bilirubin, positive cephalin flocculation, and normal alkaline phosphatase values were observed at the height of the infection. Early in October, her appetite improved, and all clinical evidence of hepatitis disappeared by the end of November, 1950.

TABLE 2.—*Data on Recipients*

Case	Recipient and Age, Yr.	Sex and Race	Reason for Transfusion	No. of Donors	Onset of Hepatitis After Transfusion, Days
1	F. M. 66	F W	Transverse colectomy for polyposis	1	65
2	L. G. 40	F W	Mastectomy for carcinoma of breast	1	48
3	M. G. 41	F W	Operation for retroversion of uterus, benign ovarian cysts, and rectocele	1	40
4	M. W. 83	M W	Hematemesis, origin undetermined	1	53
5	L. K. 69	M W	Suprapubic prostatectomy for benign hypertrophy	1	70
6	E. H. 50	F W	Extraction of third molar	1	68
7	I. M. 60	M W	Suprapubic prostatectomy for benign hypertrophy	1	44
8	B. S. 32	M W	Anemia, cause undetermined	1	32
9	E. C. 21	F N	Operation for ectopic pregnancy	2	59
10	J. G. 41	F N	Colectomy for ulcerative colitis	2	60
11	R. C. 21	F N	Excision of nodular goiter and cervical lymph nodes	2	a-82* b-20*
12	E. C. 40	F N	Hysterectomy, bilateral salpingo-oophorectomy, and appendectomy and endometriosis for leiomyomas	2	111
13	W. B. 19	M W	Colectomy for chronic ulcerative colitis	3	71
14	R. C. 34	F W	Cesarean section	3	86

* This recipient received two transfusions; one 82 and one 20 days before the onset of hepatitis.

DONOR 2.—L. H., a 25-year-old man, when reexamined on Sept. 28, 1950, 84 days after donation, gave a history of surgical repair of the intestines after a knife wound in 1942.

6. Neefe, J. R., and others: Studies on the Incidence and Nature of Hepatic Disturbance Following Acute Viral Hepatitis with Jaundice, to be published. Neefe, J. R., and Gambescia, J. M.: Diagnosis of Liver Disease, M. Clin. North America **35**: 1649 (Nov.) 1951.

Although not known, he may have received a transfusion at that time. An unexplained episode of weakness, fever, and anorexia of several days' duration occurred about four months prior to donation of blood for recipient 2. He drank beer and whisky for periods of several days at a time. During these episodes, his diet was thought to be irregular. On physical examination, his liver was palpable 2 cm. below the right costal margin and was firm and smooth. Results of laboratory studies as shown in table 3 were normal, except for the value of zinc turbidity that fell in the equivocal range.

Fig. 1 (donor 2).—Photomicrograph of liver biopsy from proved carrier showing a slight increase of collagenous connective tissue and moderate round cell infiltration of one portal area (× 120).

Repetition of the tests on Oct. 18, 1950, and on July 26, 1951, also gave equivocal results. On Aug. 2, 1951, one year and 27 days after donation, sulfobromophthalein sodium retention was 14%. This was the only abnormal measurement.

A needle biopsy of the liver on Dec. 28, 1950, nearly six months after donation, showed that the lobular structure was preserved, but was slightly distorted by increased amounts of collagenous connective tissue in the periportal areas (fig. 1). The periportal areas were also heavily infiltrated with lymphocytes and mononuclear phagocytes. There were no bile casts in the bile ducts or bile canaliculi. The size and shape of the parenchymal cells were generally normal, and most of them contained visible glycogen. Some of the cells, particularly in the periphery of the lobules, were distended with fat vacuoles. There were no areas of necrosis.

RECIPIENT 3.—M. G., a 41-year-old woman, was operated on on Aug. 10, 1950, for prolapse and retroversion of the uterus, benign ovarian cysts, and rectocele. During the operation, she received one transfusion of 500 ml. of blood. Postoperative convalescence was uneventful. On Sept. 19, 1950, 40 days after transfusion, she felt nauseated, and several days later she began to vomit, became jaundiced, and noticed dark urine and light stools. Pruritus was an additional symptom. The liver was reported as being enlarged and tender. She was hospitalized elsewhere and for the next three months suffered intermittently from the symptoms mentioned. Convalescence thereafter was prolonged.

DONOR 3.—V. S., a 32-year-old man, when reexamined on Oct. 4, 1950, 63 days after donation of blood, stated that he received intramuscular treatment, presumably antisyphilitic, for six months in 1942. He entered the U. S. Army in 1943 and received numerous inoculations. He served in the southwest Pacific, the Philippines, and Okinawa. He stated that he had been drinking alcoholic beverages since the age of 12, but that during service in the Army and thereafter he had been drinking more heavily, especially on weekends. The history suggested that his protein intake was inadequate. His wife and two children were living and well and had had no attacks of jaundice. During this period, the donor was well, except for a mild attack of anorexia and fever about five months before donation of blood. On physical examination, the liver edge was palpable 1 cm. below the costal margin and was firm, smooth, and nontender. The results of laboratory tests (table 3) show equivocally increased values for total serum bilirubin, zinc turbidity, and thymol flocculation at pH 7.55. The thymol turbidity at this pH was definitely increased and was considered positive. Although there were variations in results, some of the tests were considered positive on repetition on Oct. 19, Nov. 11, and Nov. 14, 1950, and Aug. 7, 1951, more than one year after donation. The sulfobromophthalein sodium retention at times was as high as 15.7%.

On Nov. 14, 1950, 104 days after donation, a needle biopsy of the liver was done. This showed that the lobular architecture of the liver was preserved, but slightly increased

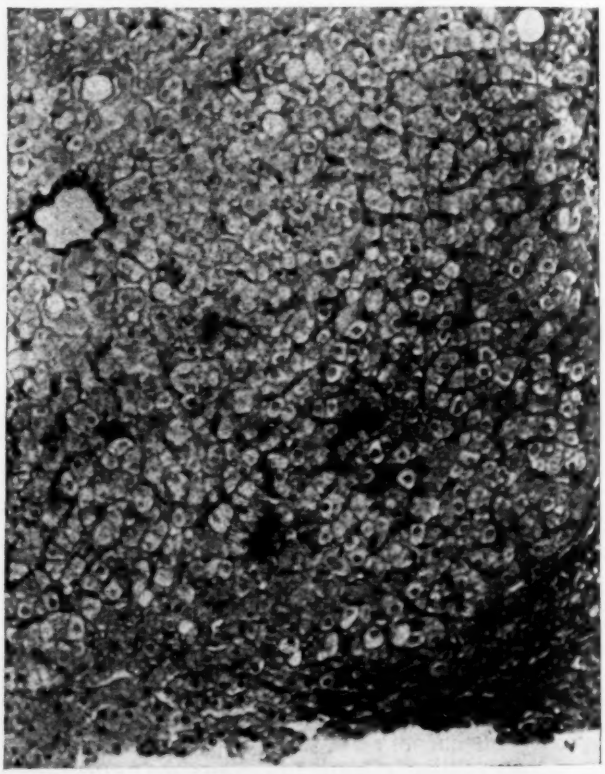

Fig. 2 (donor 3).—Photomicrograph of liver biopsy from proved carrier showing a questionable increase in collagenous connective tissue and moderate round cell infiltration of one portal area (× 120).

amounts of collagenous connective tissue were present in the periportal spaces accompanied by infiltration with lymphocytes and mononuclear phagocytes (fig. 2). The bile ducts were not proliferating abnormally. A bile cast was seen in one bile duct. Casts were not observed in any of the canaliculi. The parenchymal cells were normal in size and shape and usually contained normal amounts of glycogen. Many of the cells, especially in the periportal areas, contained large and small globules of fat.

RECIPIENT 5.—L. K., a 69-year-old man, had a suprapubic prostatectomy on Jan. 30, 1951, for benign hypertrophy of the prostate and at that time received one transfusion of 500 ml. of blood. Convalescence was uneventful. On April 25, he was readmitted because of jaundice that appeared on that day. He stated that on April 10, 70 days after transfusion, he noticed anorexia and indigestion, darkening of the urine, and penile and scrotal pruritus. Intermittent dull aching pain was present in both upper quadrants of the abdomen. The medical history was not revealing, except that the man had drunk whisky daily for 30 years. On examination, he was deeply jaundiced and the liver, which was smooth and tender, extended 5 cm. below the costal margin. There was an itching papular eruption of the scrotum. The patient soon improved and was discharged on May 31. Results of laboratory studies were also compatible with a diagnosis of viral hepatitis.

5, 1951. At this time he received a single transfusion of 500 ml. of blood. Convalescence was uneventful, except for a mild attack of phlebitis in the left leg. During a follow-up examination on May 19, 44 days after transfusion, tenderness in the right upper quadrant of the abdomen was observed. He was readmitted to the hospital on May 31, complaining of jaundice, anorexia with occasional vomiting, light stools and dark urine, and fatigue of several days' duration. The liver, which was palpable 4 cm. below the costal margin, was firm, smooth, and tender. Clinically the condition of the patient soon improved, and he was discharged on June 15 with a diagnosis of viral hepatitis. The results of laboratory tests were compatible with this diagnosis.

DONOR 7.—H. H., a 22-year-old man, when reexamined on June 14, 1951, 85 days after donating blood to recipient 7, gave no history of serious illness or of any disorder sugges-

TABLE 3.—*Data on Donors*

Case	Donor	Age, Yr.	Sex	Interval After Donation, Days	Total Serum Bilirubin, Mg./100 Ml.	Serum Bilirubin, Mg./100 Ml. in 1 Min.	pH 7.8		pH 7.55		Cephalin-Cholesterol Flocculation		Zinc Turbidity, Units	Urine Urobilinogen, Ehrlich Units	Sulfobromophthalein Retention, %	Date of Tests
							Thymol Turbidity, Units	Thymol Flocculation	Thymol Turbidity, Units	Thymol Flocculation	24 Hr.	48 Hr.				
1	W. C.	28	M	111	0.48	....	1.3	0	6.4*	0	0	..	14.2†	.....	.....	10/ 6/50
2	L. H.	25	M	84	0.12	0.02	1.3	0	2.2	0	0	0	10.8	.....	5.4	9/28/50
3	V. S.	32	M	63	1.18*	0.16	1.3	0	10.1†	1+*	0	0	12.0*	.....	.....	10/ 4/50
4	H. J.	55	M	102	0.13	0.11	5.5*	0	11.2†	0	0	0	13.4†	0.42	18.0† (2/13/51)	2/ 1/51
5	R. F.	37	M	114	1.20*	0.14	2.6	1+*	8.1†	2+†	0	0	7.2	.....	.....	5/ 8/51
6	J. G.	49	M	101	0.44	0.85	2.0	0	5.5*	0	0	0	4.6	0.46	6.2 (6/ 1/51)	5/24/51
7	H. H.	22	M	85	0.50	0.07	3.5	0	6.2*	3+†	2+†	3+†	8.0	.....	10.3† (8/ 3/51)	6/14/51
8	C. D.	36	M	43	0.38	0.20	18.7†	3+†	22.8†	3+†	0	1+*	20.0†	0.47	5.8 (1/17/52)	8/29/51
9a	L. G.	35	M	287	0.44	0.02	1.8	0	1.8	0	0	0	5.6	0.30	10.0†	10/24/50
b	A. D.	32	M	294	0.44	0.13	11.9†	0	15.2†	0	0	0	12.2*	0.68	3.1 (12/ 9/50)	11/ 1/50
10a	T. E.	28	M	226	0.64	0.09	2.2	0	3.3	0	0	0	7.0	0.21	3.4 (7/28/51)	10/27/50
b	F. A.	49	M	226	0.76	0.09	2.6	0	5.1	0	0	0	9.6*	0.44	.....	10/31/50
11a	D. S.	37	M	122	0.38	0.11	4.8*	0	7.0†	0	0	0	10.0*	0.36	18.4†	2/16/51
b	C. C.	28	F	48	0.30	0.11	1.1	0	2.2	0	0	0	9.2	.....	2.1 (7/26/51)	2/ 8/51
12a	B. C.	24	M	78	1.12*	0.09	2.0	0	4.0	0	0	0	7.4	0.44	15.0†	9/28/51
b	A. M.	31	M	88	0.13	0.05	1.3	0	2.2	0	0	0	8.4	0.25	4.3	10/ 8/51
13a	R. C.	33	M	130	0.24	0.09	1.3	0	1.3	0	0	1+*	6.0	1.09	6.2 (7/29/51)	7/ 3/51
b	E. B.	36	M	124	0.33	0.06	1.3	0	1.8	0	0	0	4.2	0.60	4.6 (8/ 1/51)	7/ 6/51
c	M. S.	30	F	131	0.44	0.07	2.0	0	2.6	0	0	1+*	7.4	0.41	7.0* (8/ 3/51)	7/ 5/51
14a	F. S.	33	M	121	0.31	0.03	3.4	0	4.3	0	0	0	7.0	0.88	1.3	4/10/52
b	A. L.	39	F	130	0.47	0.07	1.9	1+*	2.4	1+*	0	0	5.4	0.49	5.4	4/19/52
c	J. E.	25	F	118	0.34	0.07	1.3	1+*	2.2	1+*	1+†	1+	3.2	0.78	.....	4/ 7/52

* Result considered equivocal.
† Result considered positive, or definitely abnormal.

A cholecystogram showed an abnormally functioning gallbladder containing calculi. Currently the patient is well.

DONOR 5.—R. F., a 37-year-old tailor, when reexamined on May 8, 1951, 114 days after donation of blood, stated that he had always been in good health, except for occasional colds, and gave no history suggestive of an attack of viral hepatitis. As a professional donor, he had numerous stylet punctures of the finger for hemoglobin estimations. He stated that he drank two bottles of beer and one highball a week. On physical examination, the edge of the liver was just palpable below the costal margin and was firm and nontender. The remainder of the physical examination was essentially normal. Laboratory studies (table 3) indicated an equivocal increase in bilirubin and positive thymol turbidity and flocculation tests at pH 7.55. The donor was not available for continued follow-up.

RECIPIENT 7.—I. M., a 60-year-old government inspector, had diabetes for a number of years and had a suprapubic prostatectomy for benign hypertrophy of the prostate on April

tive of jaundice. As a professional donor, he had been subjected to numerous stylet punctures of the fingers. He had not had military service, and he denied injections or the use of alcoholic beverages. Because of the uncooperative attitude of the patient, however, the reliability of the history is questionable. He was said later to have been detained by police as a suspected narcotic addict. On physical examination, which was otherwise normal, the edge of the liver could be readily palpated just below the costal margin and was firm, round, and nontender. Laboratory tests (table 3) showed an equivocal thymol turbidity and a positive thymol flocculation at pH 7.55. Cephalin-cholesterol flocculation was positive at 24 and 48 hours. When examined again on Aug. 3, 1951, 135 days after donation, the cephalin-cholesterol and thymol flocculation were normal. Thymol turbidity at pH 7.55 continued positive and at pH 7.8 was equivocal. Sulfobromophthalein sodium retention measured at another hospital was positive. On Oct. 16, 1951, 209 days after the original donation, he had an attack of viral hepatitis with jaundice. He was admitted to another

hospital from which he was discharged early in November. Convalescence appeared uneventful, but results of the hepatic function tests remained abnormal. A follow-up will be reported elsewhere.

RECIPIENT 8.—B. S., a 32-year-old man, was first admitted to this hospital in April, 1951, for investigation of hypertension. He was readmitted on July 14 to the orthopedic service for biopsy of the right ilium. The pathological diagnosis was localized osteitis fibrosa cystica. Because the patient was considered anemic, he was given a single transfusion of 500

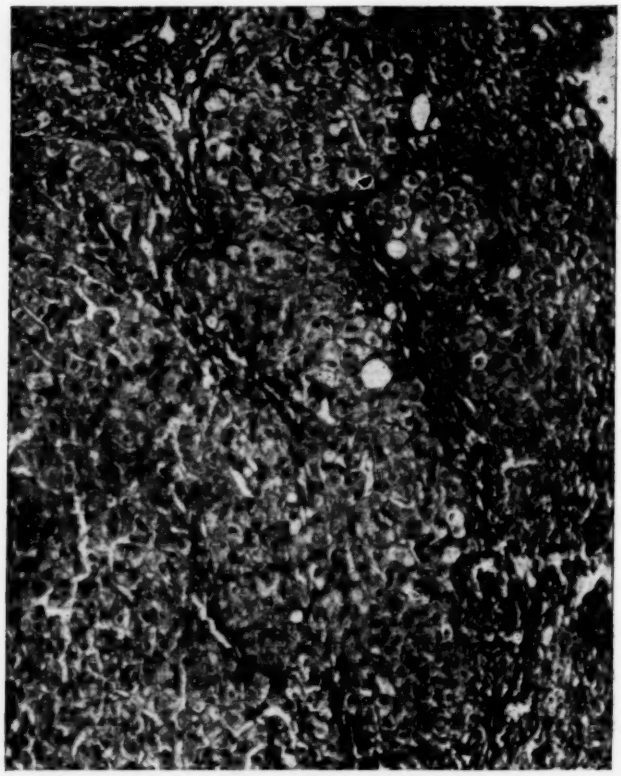

Fig. 3 (donor 8).—Photomicrograph of liver biopsy from proved carrier showing extensive scarring and distortion of the lobular pattern. The scars are infiltrated with chronic inflammatory exudate. Nodular regeneration of the parenchymal cells is evident (× 95).

ml. of blood. Convalescence was uneventful. He was well until about Aug. 18, 1951, 32 days after transfusion, when he first began to feel weak and to have no appetite. On Aug. 21, he noted that his stools were light and his urine was dark. By Aug. 25, he was obviously jaundiced, and, therefore, he was admitted to the medical service on Aug. 28. On reexamination, in addition to jaundice, it was found that the liver edge was palpable 6 cm. below the costal margin and was smooth and firm, but not tender. Blood pressure was 160 systolic and 100 diastolic. The illness progressed favorably, and the man was discharged much improved on Sept. 10. The final diagnosis was viral hepatitis. Laboratory data were compatible with this diagnosis.

DONOR 8.—C. D., a 36-year-old man, when reexamined on Aug. 29, 1951, 43 days after donation, stated that he had had intermittent epigastric fulness and bloating for several years. In April, 1951, he had an acute febrile illness, without jaundice, characterized by headache, malaise, and weakness that persisted for several days and for which he was treated with penicillin injections. Following this illness, the epigastric symptoms were severer, his appetite was diminished, and he was easily fatigued. Although his diet appeared adequate, he stated that for many years he had consumed up to one pint of whisky and several bottles of beer a day. He was formerly employed as a roofer, but since April, 1951, he had worked as a bartender. On examination, the liver edge, which was smooth, firm, and slightly tender, was palpated 4 cm. below the right costal margin. Several spider angiomas were seen. Laboratory data (table 3) showed positive measurements in the case of thymol turbidity and flocculation tests at both pH 7.8 and 7.55 and a positive zinc turbidity test. About four months later, sulfobromophthalein sodium retention was also abnormal. During the 10 months following donation, he was reexamined on eight occasions. There were only minor fluctuations in the results at subsequent examinations. Meanwhile the donor stopped drinking whisky and beer and reported a great improvement in his sense of well being.

On Nov. 2, 1951, a needle biopsy of the liver showed that the structure was greatly distorted by scarring and nodular hyperplasia of the parenchymal cells (fig. 3). Associated with wide bands of dense collagenous tissue were small numbers of lymphocytes and plasma cells. There was no acute inflammatory exudate. Although most of the parenchymal cells contained glycogen, some of them were distended with large fat vacuoles. The bile canaliculi and intrahepatic bile ducts did not contain inspissated bile, and there were no iron deposits.

DONOR 12a.—B. C., a 24-year-old man, had blood drawn for hepatic function tests at a blood donation on July 12, 1951. Because of total serum bilirubin value of 1.72, the only

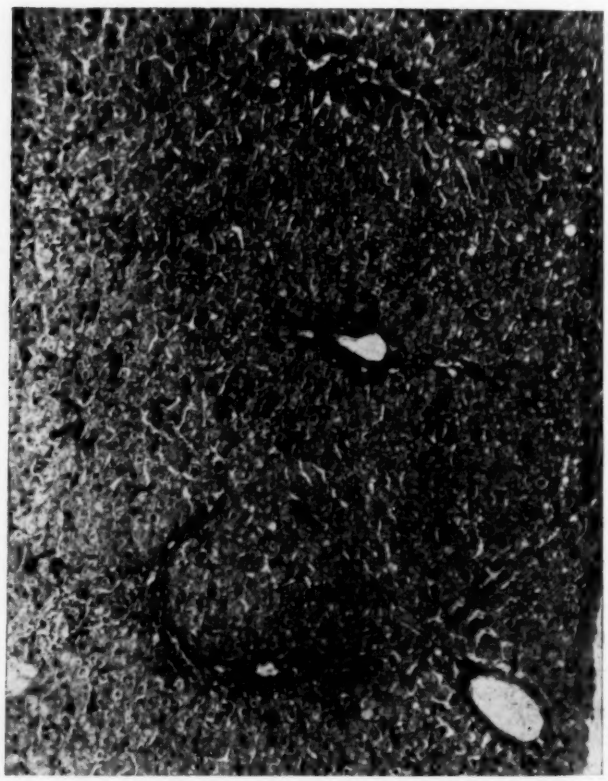

Fig. 4 (donor 12a).—Photomicrograph of liver biopsy from suspected carrier showing slight distortion of the lobular pattern as the result of increased amounts of collagenous connective tissue and infiltration with chronic inflammatory exudate in one portal area (× 76).

abnormal test, he was recalled for reexamination on Sept. 28, 1951, 78 days after donation, but five weeks before the recipient of his blood became jaundiced. At this time, he gave no history of previous jaundice or illness that could be ascribed to hepatic disease. On occasions in the past he had been inoculated with various immunizing agents. The last injection

was with tetanus toxoid in July, 1950. His diet appeared to be adequate, but he drank regularly. Results of physical examination were essentially normal. The results of hepatic function tests at this time are shown in table 3. The total serum bilirubin value was now in the equivocal range, but sulfobromophthalein sodium retention, measured for the first time, was greatly increased. The patient was not available for follow-up until Feb. 25, 1952, 229 days after donation and more than three months after the recipient of his blood became jaundiced. At this time, the thymol turbidity at pH 7.55 was positive. The sulfobromophthalein sodium retention was now normal. On March 8, 1952, a needle biopsy of the liver was performed. There was slight distortion of some periportal areas as the result of slight proliferation of collagenous tissue and infiltration with chronic inflammatory cells. Also observed were slight increases in the amount of fat in some of the parenchymal cells (fig. 4).

COMMENT

The ages of the recipients, as shown in table 2, varied from 19 to 83 years. Whether any of the listed illnesses or operations of the recipients predispose them to viral hepatitis is unknown, although the fact that three patients had colectomies, of which two were for ulcerative colitis, is of interest. In two instances, viral hepatitis followed transfusion associated with suprapubic prostatectomy.

The period of time between transfusion and the onset of hepatitis varied between 20 and 111 days. Recipient 11 had received two transfusions, 82 and 20 days, respectively, before the onset of hepatitis. The laboratory data for the two donors (table 3) suggest that the transfusion responsible for the hepatitis was the first rather than the second. The shortest interval, therefore, might be 32 days (recipient 8) instead of 20 days. In any event, the range of incubation periods observed are compatible with one or the other of the ranges associated with either the IH (15 to 60 days) or SH (45 to 180 days) type of hepatitis virus.[4a] The possibility that the infection in some recipients may have resulted from contaminated syringes, needles, blood lancets, etc. seems unlikely as the regulations of this hospital forbid the use of such instruments in two patients without heat sterilization between each use. That several of the recipients may have had naturally acquired infections or other transient causes of jaundice cannot be excluded, but this seems unlikely.

Worthy of emphasis is the fact that none of the donors, when questioned again at reexamination, admitted previous jaundice, although several recalled nonspecific, transient illnesses that might possibly have represented viral hepatitis without jaundice. Except for minor, nonspecific transient complaints, all felt well enough to continue their usual occupations.

In respect to those donors from whom needle liver biopsies were obtained, the photomicrographs of the specimens from donors 2, 3, and 12a (fig. 1, 2, and 4) show only slight distortion of the lobular structure and small amounts of chronic inflammatory exudate in the periportal areas. Whether in some cases these lesions may progressively increase to a stage of unequivocal chronic hepatitis or cirrhosis is uncertain. In the case of donor 8 (fig. 3), however, there is sufficient scarring, distortion of the lobular structure, and parenchymal cell regeneration to classify this combination of lesions as cirrhosis. In view of the sparsity of fatty infiltration, the presence of chronic inflammatory exudate in the areas of fibrosis, and the limitations of a needle biopsy specimen, more specific classification as either post necrotic or Laennec's cirrhosis does not seem justifiable. Donors 2, 3, and 8 are proved carriers.

Referring to the eight single donors, those who donated blood for the eight patients with hepatitis who received blood from only one donor (table 3), the fact that six of the eight had at least one positive and one equivocal hepatic test at the time of reexamination deserves emphasis. With respect to the other two single donors (for recipients 2 and 6), one hepatic test was equivocal in each. At least one of the two donors for three of the four recipients (9, 11, and 12 in table 3) who each received blood from two donors had a minimum of one positive and one equivocal hepatic function test. In case 10 (described in tables 2 and 3 only), one of the two donors had one equivocal test. In neither of the recipients who received blood from three donors did any donor have a positive hepatic function test at the time of reexamination, except donor 14c. In this instance, a cephalin-cholesterol flocculation positive after 24 hours, but normal in 48 hours, was discounted. Donor 13c had one equivocal test. Of interest, however, is the fact that one or more of the donors for each of the two recipients (13 and 14 in table 2) had definite histories of exposure to hepatitis. Also of interest is the fact that in donor 12a results of tests made on an aliquot of the blood collected at the time of original donation for recipient 12 were abnormal.

SUMMARY AND CONCLUSIONS

The occurrence of viral hepatitis in 14 recipients of whole blood transfusions is reported. Eight recipients received one unit of 500 ml. of whole blood; four received two units; and two received three units. None of the donors had a history of jaundice or recognized hepatitis. When examined after the onset of hepatitis in the recipients at least one of the donors for 9 of the 14 patients in whom post-transfusion hepatitis developed had sufficient alteration of one or more hepatic function tests to suggest the presence of hepatic disturbance. Final proof of a relationship between such hepatic disturbance and a blood carrier state of hepatitis virus, except for circumstantial evidence of hepatitis in the recipients, depends on the demonstration of the presence of hepatitis virus in the donor's blood by transmission experiments in human volunteers. Since the supply of volunteers for such experiments is limited, only the eight donors for recipients who received a single transfusion were considered for such tests. Specimens of blood serum from donors 1, 2, 3, 5, 7, and 8 were selected for transmission experiments. Descriptions of these experiments follow in part 2 of this paper.

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2. CONFIRMATION OF CARRIER STATE BY TRANSMISSION EXPERIMENTS IN VOLUNTEERS

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In view of the observations that post-transfusion hepatitis developed in 14 recipients of whole blood, proof of a relationship between such hepatic disturbances and a blood carrier state of hepatitis virus in the donors was sought. Although much evidence supporting such a carrier state was obtained from laboratory tests, it was felt that final proof could be obtained only in the results of transmission experiments carried out in human volunteers. Eight donors, for recipients who received a single transfusion and in whom hepatitis later developed, were chosen for these tests. Blood serum was collected from donors 1, 2, 3, 5, 7, and 8 (described in detail in part 1 of this paper) at the most recent follow-up examination (table 4) in order to provide a maximum time interval between the original donation, which was followed by hepatitis in the recipient, and the transmission experiments. With respect to the serum specimens from donors 2 and 3, three specimens from each were collected at approximately weekly intervals and were pooled for these experiments because of the possibility that viremia might be intermittent. In the remaining donors, single specimens were used for the experiments.

MATERIALS AND METHODS

The men participating in the studies were inmates of federal penitentiaries; the men volunteered for this purpose. All volunteers were carefully screened in order to eliminate those whose health might be unnecessarily jeopardized and to make sure that in all the results of tests and the other factors used as criteria in detecting the onset and course of viral hepatitis were normal. The age limits were set at between 21 and 35 years. On the basis of history and physical examination, volunteers were rejected if there was any evidence of disease or if there was a history of liver disease. Hepatic function tests shown in table 1 of part 1 of this paper, except for the sulfobromophthalein sodium retention test, were performed routinely on specimens from each volunteer. In addition, the phenol turbidity and urine bilirubin reactions [1] were also performed.

After inoculation, the subjects were seen at least once a week by the physician assigned to the respective institution for the purpose of this study. The subjects were questioned about symptoms of hepatitis and given a physical examination. Particular attention was paid to the development of hepatomegaly, splenomegaly, icterus, and abdominal or epigastric tenderness. When indicated, the examinations were conducted at more frequent intervals. When sustained symptoms, physical abnormalities, or positive results of hepatic tests were observed, the volunteer was hospitalized for observation and treatment. Frequently, the onset of clinical hepatitis was anticipated by the earlier occurrence of abnormal results of hepatic tests. Once a subject was hospitalized, hepatic function tests were done more frequently until convalescence was complete. The hepatic function tests served as aids to clinical judgment in determining when a subject should be discharged from the hospital. In any event, whether they became ill or not, volunteers were kept under weekly observation for a minimum of five or six months and for longer periods if any abnormalities persisted.

Hepatic function tests on blood serum from the volunteers were carried out at the National Institutes of Health, Bethesda, Md. Specimens were sent to Bethesda from the penitentiaries by the speediest means available and usually arrived within 24 to 36 hours after collection. Tests on specimens of urine were made in the penitentiary hospitals.

Specimens of blood serum for inocluation were transmitted, packed in dry ice, by special messenger from the Hospital of the University of Pennsylvania to the National Institutes of Health where they were stored at −18 C. When later transported for inoculation purposes, specimens were packed in dry ice and were personally carried by the medical officer who superintended the inoculations.

The volunteers were divided into 6 groups of 10 men each for studying the serum from each of the 6 donors. Each volunteer was inoculated subcutaneously with 1 ml. of serum. Table 4 shows that the materials from donors 2 and 3 used for inoculation consisted of homologous pools of three serums collected at weekly intervals from each donor, whereas materials from the other donors used for inoculation consisted of single specimens. Two additional groups of volunteers were subsequently inoculated with portions of serum remaining from the original specimens obtained from donors 2 and 7. This was done as part of another study that will be reported elsewhere.[2]

RESULTS

Except for the group of patients inoculated with serum from donor 1, acute hepatitis developed in at least one volunteer in each group after an interval compatible with the incubation period of the IH or SH type of viral hepatitis. The results of hepatic function tests in each instance supported the diagnosis. In four of the groups, additional volunteers had illnesses believed to be viral hepatitis without jaundice. The diagnosis was supported by the results of the hepatic function tests. In general, the intervals between inoculation and the onset of hepatitis in the vol-

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The service rendered by the volunteers is gratefully acknowledged.

† Deceased.

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2. Murray, R., and others: To be published.

unteers corresponded with the time interval between the original transfusion and the occurrence of hepatitis in the recipients. In view of the closer observation of the volunteers during the preicteric period, however, it is to be expected that these figures would be smaller. In groups receiving serum from donors 7 and 8, the variation was such that some figures corresponded with the incubation period of infectious hepatitis and others with that of homologous serum hepatitis.

COMMENT

The failure of serum from donor 1 to cause viral hepatitis in the volunteers may be ascribed to any one of a number of causes. 1. The original recipient of the blood transfusion may have acquired viral hepatitis from another source. 2. Viremia may have been transitory and the blood of the donor, when drawn for transmission experiments 203 days after the original donation, may have been no longer infectious. 3. Even in persons harboring the virus of hepatitis for long periods, viremia may be intermittent. 4. All of the volunteers may have been immune to this particular strain of virus. 5. The serum inoculated may have been infectious originally, but the virus may have been inactivated in the course of handling and storage.

TABLE 4.—*Results of Inoculation of Volunteers with Serum from Suspected Donors*

Case	Donor	Date of Donation Suspected	Dates of Serum Collection	Minimum Interval, Days	Dates of Inoculation	No. of Inoculations	Cases of Hepatitis: With Jaundice	Cases of Hepatitis: Without Jaundice	Cases of Hepatitis: Total	Incubation Period, Days: In Volunteers *	Incubation Period, Days: Original Recipient
1	W. C.	6/16/50	1/ 5/51	203	8/24/51	10	0	0	0	.....	65
2	L. H.	7/ 6/50	7/26/51 8/ 2/51 8/ 9/51	385	8/24/51 7/ 3/52	10 5	4 0	2 † 1	6 1	(18), 30, 45, 46, (46), 56 (43)	48
3	V. S.	8/ 2/50	7/24/51 7/31/51 8/ 7/51	356	8/24/51	10	1	0 †	1	48	40
5	R. F.	1/14/51	6/12/51	149	8/24/51	10	1	0 †	1	84	70
7	H. H.	8/21/51	8/ 3/51	135	8/24/51 7/ 3/51	10 5	4 5	0 ..	4 5	35, 50, 56, 72 43, 49, 56, 57, 63	44
8	C. D.	7/17/51	8/29/51	43	4/ 7/52	10	2	1 ‡	3	(50), 57, 67	32

* Incubation periods in parentheses refer to cases of hepatitis without jaundice.
† One additional subject in this group had equivocal or abnormal hepatic tests suggestive of hepatitis without jaundice.
‡ Three additional subjects in this group had equivocal or abnormal hepatic tests suggestive of hepatitis without jaundice.

The evidence indicates that at least five of the six donors tested were asymptomatic carriers of hepatitis virus. Inspection of the intervals between the time of donation and the time at which samples were obtained for transmission experiments shows that the minimum known periods of infectivity varied from 43 to 385 days. The long intervals suggest that some persons may be carriers of the virus for even longer periods. That this may be the case is shown by the report of Berk and Malamut [3] that suggests that one professional donor was the source of infection in recipients of his blood over a period of at least five and one-half years.

None of the present donors was known to have had a previous attack of viral hepatitis with jaundice. Although the number of proved carriers among the 22 studied is limited to 5, specific comment on the pertinent data referable to these 5 donors appears warranted. Three of the five were professional donors, and four admitted excessive alcohol intake. In only one (donor 7) of the 22 donors, a proved carrier, did jaundice develop after his blood had been shown to be infectious (seven months after donation for the original recipient and three months after collection of the blood tested in the volunteers; see case report for donor 7 in part 1 of this paper).

If the incubation periods are considered suggestive of the type of hepatitis virus concerned,[4] it appears that both the IH and SH type of hepatitis virus may be associated with the carrier state. This evidence is inconclusive, especially in view of the wide spread of incubation periods, overlapping the ranges of the IH and SH type of virus, in the volunteers injected with serum from donors 7 and 8. The explanation for this variation is not known, although it is entirely possible that other as yet unrecognized types of hepatitis virus may exist or modification of the IH or SH type may occur. It may even be as MacCallum suggests, that incubation is related to the presence of both agents in one person. The type of virus concerned in post-transfusion hepatitis has some practical significance in view of the effective prevention or modification of the IH type of viral hepatitis by gamma globulin when administered prior to the onset of the disease.[5] It is of interest to note that the incubation periods for 4 of the 14 original recipients were under 50 days and under 60 days for 6 of the recipients. Incubation periods in this range, particularly under 50 days, are more apt to be associated with the IH type of virus. If the incubation periods of the present group of 14 patients are representative, 28 to 42% of infections from whole blood possibly may be due to the IH type of virus. Theoretical reasons of why a higher incidence of the IH type of infections might be expected with whole blood than with plasma have been discussed previously by Neefe.[6] Such an incidence of the IH type of infections might justify consideration of post-transfusion prophylaxis with gamma globulin as a further potential aid in the reduction of the incidence of this serious complication. The available supply of gamma globulin, however, is a limiting factor in this respect at the present time.

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5. Stokes, J., Jr., and Neefe, J. R.: Prevention and Attenuation of Infectious Hepatitis by Gamma Globulin: Preliminary Note, J. A. M. A. **127**: 144 (Jan. 20) 1945.

6. Neefe, J. R.: Recent Advances in the Knowledge of "Virus Hepatitis," M. Clin. North America **30**: 1407 (Nov.) 1946.

At the time of the first examination of the six single donors (donors 1, 2, 3, 5, 7, and 8) after the occurrence of viral hepatitis in the recipients of their blood, only donor 2 did not have one or more positive hepatic tests. When blood was drawn again 301 days later for transmission experiments, the serum of this donor was still infectious, as shown by the occurrence of viral hepatitis in five of the volunteers. During the interval, although the zinc turbidity became normal and remained so, the sulfobromophthalein sodium retention gradually increased until, at that time, it was 14%. This course of events suggests that although viremia is not always associated with sufficient disturbance of hepatic function to be detected by the usual hepatic tests, progressive or intermittent hepatic injury, subsequently reflected by abnormal test results, may occur in association with a prolonged carrier state.

By contrast, donor 1, who had a positive zinc turbidity and an equivocal thymol turbidity (at pH 7.55) 111 days after donation of blood, also had approximately the same abnormalities of hepatic function tests at the time blood was drawn for transmission studies 92 days later. In this instance, none of the volunteers acquired overt viral hepatitis. Sulfobromophthalein sodium retention was not measured in this donor because he would not cooperate.

With respect to the four other donors, fluctuation in the results of hepatic function tests occurred over a period of time. At each follow-up examination however, certain test results were positive. A more detailed report of the serial laboratory studies on the carriers is planned for the future.

From the evidence presented, therefore, it may be concluded that many, but not all, carriers of hepatitis virus will have an abnormal result in one or more hepatic function tests. Such abnormalities apparently may vary in degree and may be intermittent. Obviously, such abnormal test results will be obtained in many persons with hepatic or other diseases that have no relationship to hepatitis virus.

When the results of hepatic tests are inspected (table 3 of part 1), it is evident that results of the thymol turbidity, zinc turbidity, and sulfobromophthalein sodium retention tests were abnormal more frequently than those of the other tests. The thymol reagent buffered at pH 7.55 was more dependable in this respect than that buffered at pH 7.8. The sulfobromophthalein test is not practical for routine screening. A screening program limited to the thymol (buffered at pH 7.55) and zinc turbidity tests, however, might be a suitable method for eliminating some potentially infectious donors. A study concerning the routine testing of blood donors, at the time of donation, is in progress and will be reported elsewhere.[7]

7. Fitch, D. R., and others: Incidence of Suspected Hepatic Disease in Asymptomatic Blood Donors: Possible Relation to Carrier State of Viral Hepatitis, abstract of Chicago meeting of American Society of Clinical Pathologists, Oct. 8, 1952, to be published.

8. Ginzburg, L.; Sussman, L. N., and Auerhan, H.: Posttransfusion Viral Hepatitis as a Surgical Complication, Surg., Gynec. & Obst. 92: 492 (April) 1951.

9. Perkins, R. F.; Baggenstoss, A. H., and Snell, A. M.: Viral Hepatitis as a Cause of Atrophy and Cirrhosis of the Liver, Proc. Staff Meet., Mayo Clin. 25: 287 (May 24) 1950.

Ginzburg and his associates [8] have recently reported studies on two donors who were presumed to have been the source of infection in two and three patients respectively in whom homologous serum hepatitis occurred after receiving whole blood transfusions from the two donors. Both donors, although asymptomatic, were found to have abnormal values for the cephalin-cholesterol flocculation and thymol turbidity reactions.

The occurrence of round cell infiltration and slight proliferation of connective tissue in the liver biopsies of three donors, two of whom were proved carriers, and the marked scarring and nodular regeneration of the liver in the fourth donor, also shown to be a carrier, suggest that long-sustained infection, without a preceding episode of recognized acute hepatitis with jaundice, may play an etiological role in some patients with insidiously developing chronic liver disease. Preceding acute hepatitis with jaundice is generally accepted as an occasional cause of cirrhosis.[9] However, the development of a chronic hepatic disease associated with a carrier state has not been clearly recognized. Also, the possibility cannot be excluded that a previously diseased liver may be more susceptible to the hepatitis virus than a normal one, the effect of hepatitis virus on such a diseased liver possibly differing from that on the normal liver.

When questioned in detail, many of the donors reported here were found to have a history of exposure to jaundice or to have had an unexplained transitory illness prior to blood donation. It seems probable that such nonspecific phenomena, except for history of jaundice or hepatitis, would be frequent among routine donors and could hardly be used as a basis for their exclusion as donors. Donors who receive payment might be expected to deny any history that would affect their acceptance as a donor. More objective methods than the history are essential for better control of this problem.

SUMMARY AND CONCLUSIONS

Blood serum was obtained from six donors at intervals of 43 to 385 days after a blood donation suspected of causing viral hepatitis in the recipients. When six groups of human volunteers were inoculated, viral hepatitis occurred in one or more volunteers in five of the six groups. This is believed to constitute proof of an asymptomatic blood carrier state for hepatitis virus. The data suggest that the routine screening of blood donors by means of certain hepatic function tests might exclude a significant number of potentially infectious carriers.

The lesions observed in liver biopsies of four donors, three of whom were proved carriers, suggest that the hepatitis virus may play a role in the pathogenesis of certain insidiously developing chronic hepatic diseases. Sometimes possibly these hepatic diseases culminate in cirrhosis, in the absence of an initiating overt attack of acute hepatitis with jaundice. The incubation periods of the post-transfusion hepatitis in the 14 original recipients suggest that IH type hepatitis virus may have been responsible for some of the infections acquired from whole blood.

DOES VASCULAR DAMAGE FOLLOW TOXEMIA OF PREGNANCY?

AN INTERNIST'S APPRAISAL OF THREE HUNDRED THREE PATIENTS IN A TOXEMIA CLINIC

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In July, 1952, in conjunction with the obstetric department, a toxemia clinic was instituted at the Gallinger Municipal Hospital. The main reason for organizing the clinic was to find out what happened to toxemia patients after they left the hospital. How beneficial was our hospital therapy? Did vascular damage follow toxemia? It soon became apparent, however, that here was an excellent opportunity to study the patient with toxemia from the onset of toxemia symptoms in midpregnancy, throughout the remainder of her pregnancy, then in the hospital, and finally back in the toxemia clinic until all signs and symptoms of toxemia had disappeared. For this reason, then, at the first sign or symptom of toxemia, the patient was transferred from the regular prenatal clinic to the toxemia clinic, where she was seen once a week until term or until hospitalization was advised. Post partum, the patient was seen at three weeks, six weeks, three months, and six months.

Besides the usual obstetric examination, including weekly blood pressure determinations and urinalysis, an ophthalmoscopic examination with the pupils dilated was performed at each visit. An analysis of the first 303 cases is the subject of the present report. The diagnoses for the 303 patients seen in the toxemia clinic were hypertensive vascular disease, 216; hypertensive vascular disease plus superimposed toxemia, 28; postpartum hypertension, 14; and true toxemia, 45. Our diagnostic criteria are given below.

HYPERTENSIVE VASCULAR DISEASE

All of the 216 patients with hypertensive vascular disease showed grade 1 or grade 2 hypertensive retinopathy (Keith-Wagner). Peripheral edema was absent or at the most 1 +; periorbital edema was absent. Albuminuria was absent or 1 +. The patients' ages ranged between 13 and 41 years, with an average age of 22 years. Although 71% of the group were multiparous, 29% were primiparous. Of interest was the fact that 20 patients (9%) were under 18 years of age. Forty-two per cent of this group of hypertensive patients had a history of "toxemia" with previous pregnancies. Since results of the examination of the optic fundi were not recorded during those earlier pregnancies, one cannot accurately state whether hypertension was present at that time.

There were 149 patients who remained hypertensive during pregnancy. It was noteworthy that the highest readings of arterial pressure consistently occurred either in the immediate postpartum period or sometime during the first two months post partum, and not at delivery as might have been expected. By three months post partum, the blood pressure had returned to its usual hypertensive level. Of the hypertensive patients, 67 (31%) became normotensive or even hypotensive during pregnancy. This group of patients was characterized by grade 2 retinopathy with a diastolic pressure of 60 to 70 mm. Hg. Immediately after delivery the patient would again become hypertensive and the blood pressure would remain elevated until the next pregnancy.

Although several excellent publications have stressed the frequency of toxemia in the young primigravid patient,[1] the frequency of hypertensive vascular disease in this group is not generally known. The overwhelming Negro population in our clinic (all except two were Negro patients) may explain, in part at least, the predominance of hypertension in this group, since hypertension is known to develop earlier in the Negro.[2] Without examination of the retinas, however, many of these patients, particularly the group under 20 years of age, would be classified as having toxemia, and the severity of the toxemia would be judged by the height of the arterial blood pressure.

The lack of correlation between arterial blood pressure and the ophthalmoscopic observations in cases of hypertensive vascular disease is well shown in the group of hypertensive patients who became normotensive in pregnancy. Dieckmann[3] and Teel[4] have occasionally witnessed this phenomenon. The cause is unknown. A clinical counterpart of this situation is occasionally seen in patients with hypertensive vascular disease in whom chronic left ventricular failure gradually develops. As soon as frank signs of failure develop in these patients, the arterial blood pressure becomes normal. The immediate return of the blood pressure to hypertensive levels after delivery certainly accounts for a fair percentage of cases of so-called postpartum toxemia or postpartum rise in blood pressure.

The presence of definite hypertensive retinopathy and the absence of a retinal sheen in a pregnant patient with an elevated blood pressure is reassuring to the physician. These patients are not toxemic; they are patients with hypertensive vascular disease who happen to be pregnant. The indications for hypotensive therapy are the same as if the patient were not pregnant, e. g., vascular damage, cerebral, cardiac, or renal impairment, and/or a rising diastolic pressure. A single elevated blood pressure reading or even several elevated blood pressure readings are

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1. Marchetti, A. A., and Menaker, J.: Pregnancy and the Adolescent, Am. J. Obst. & Gynec. **59**: 1013-1020, 1950. Schmitz, H. E., and Towne, J. E.: Adolescent Primigravida, Surg., Gynec. & Obst. **84**: 962-966, 1947.

2. Schulze, V. E., and Schwab, E. H.: Arteriolar Hypertension in American Negro, Am. Heart J. **11**: 66-74, 1936.

3. Dieckmann, W. J.: Toxemias of Pregnancy, ed. 2, St. Louis, C. V. Mosby Company, 1952.

4. Teel, H. M., and Reid, D. E.: Eclampsia and Its Sequelae: Clinical and Follow-Up Study of All Cases at Boston Lying-In Hospital over 20 Year Period, Am. J. Obst. & Gynec. **34**: 12-25, 1937.

not indications for hypotensive therapy and certainly do not indicate toxemia of pregnancy. If the blood pressure level in a woman who is not pregnant is, for example, 160/110 mm. Hg, there is no advantage in reducing this level to the recommended 140/90 mm. Hg. Our results agree with the opinion of Chesley [5] and others [6] that most hypertensive patients do well during pregnancy.

HYPERTENSIVE VASCULAR DISEASE PLUS SUPERIMPOSED TOXEMIA

There were 28 patients in this group. Their ages ranged between 14 and 31 years, with an average age of 23 years. Ten were primiparous, and 18 were multiparous. All had a history of hypertension antedating pregnancy. Examination of the retinas revealed the chronic changes of hypertension and also showed the generalized retinal sheen that is characteristic of toxemia (this will be discussed in detail elsewhere). Other signs of toxemia were also consistently present, such as edema of the ankles and periorbital area and albuminuria. Congestive heart failure was not seen.

When seen during the first trimester of pregnancy, these patients differed in no way from those who were hypertensive. The fundi showed hypertensive retinopathy with no retinal sheen; the arterial blood pressure was at the level of the nonpregnant state or lower; and no signs or symptoms of toxemia were present. Whereas signs of toxemia most frequently develop in the seventh or eighth month of pregnancy in the group with true toxemia, in this group, signs of toxemia frequently developed in the fourth or fifth month of pregnancy. A generalized retinal sheen, the first sign of superimposed toxemia, appeared in 10 patients in the middle of the fourth month, in 6 patients at five and one-half months, in 4 patients at six and one-half months, and in 8 patients at seven and one-half months. Elevation of arterial pressure (particularly the diastolic pressure), edema, and albuminuria appeared two to four weeks after the appearance of the retinal sheen, each sign increasing in severity in the subsequent month if not controlled by drug therapy. The level of arterial pressure at the height of the toxemic process was higher than in the hypertensive group or the group with true toxemia.

Three days after delivery, which was usually induced (cesarean section in 4, rupture of membranes in 16), the arterial pressure returned to the level that was normal in nonpregnant periods in 20 and remained essentially the same in 8. At three weeks post partum, there was little change in blood pressure, but there was no edema, and the retinal sheen that had been present in all at the height of the toxemic process was absent in 15 patients. A trace of albuminuria remained in four patients.

At six weeks post partum, the retinal sheen had disappeared in all patients, leaving pure hypertensive retinopathy. Edema was absent in all patients, and albuminuria was present in only the one patient who had consistently shown albuminuria prior to pregnancy. Two patients who showed grade 1 hypertensive retinopathy early in pregnancy and grade 1 retinopathy plus a generalized retinal sheen at six months gestation, showed grade 2 hypertensive retinopathy at six weeks post partum.

The frequency of hypertensive vascular disease in the young Negro woman is again seen. Our data also confirm that toxemia appears earlier in the hypertensive patient.[5a] Because of this and because of the high incidence of the severer type of toxemia in this group, the management of such patients presents a difficult problem, since the life of the fetus is always in jeopardy at this midstage of pregnancy. Early recognition of the superimposed toxemia is therefore essential. Since the appearance of the generalized retinal sheen precedes the other more obvious symptoms of toxemia (rising blood pressure and edema) by two to three weeks, its prompt recognition gives the physician an advantage in instituting therapy. Frequent ophthalmoscopic examinations in the hypertensive pregnant patient are therefore mandatory.

The finding of increased retinopathy after the toxemic episode in two patients undoubtedly represents vascular damage caused by toxemia. This seems to be related more to the duration of toxemia than to its severity.

POSTPARTUM HYPERTENSION

There were 14 patients in this group. All these patients had a completely normal pregnancy and an uncomplicated delivery with no signs or symptoms of toxemia or hypertension. Either in the immediate postpartum period (first 24 hours) or sometime within the first six weeks post partum, an elevated blood pressure reading (above 140/90 mm. Hg) was recorded. The results of ophthalmoscopic examinations were normal in all. The age of these patients ranged between 19 and 31 years. Four were primiparous, and 10 were multiparous. A history of previous toxemia or hypertension was denied by all. Five patients showed an elevated arterial pressure in the first 24 hours post partum. The blood pressure had returned to normal in two of these patients 48 hours post partum; the others returned to normal by the time of discharge from the hospital, three or four days post partum. In nine patients the first elevated blood pressure recording was made at the time of the six-week postpartum visit. Funduscopic examination was again entirely normal, and albuminuria and edema were absent. By three months post partum, the arterial pressure had returned to normal in six, and at six months post partum the arterial pressure had returned to normal in all. Again it is emphasized that a history of hypertension or toxemia or the finding of hypertension or toxemia at any time during pregnancy excluded a patient from this group. The only abnormality in this group was an elevated blood pressure reading.

Why does the arterial pressure become elevated in this period? The routine use of ergonovine (Ergotrate) after delivery may be responsible for many transient rises in blood pressure during the immediate postpartum period. When oxytocin (Pitocin) was substituted for methylergonovine tartrate in our hospital, the incidence of such immediate "postpartum rises" was greatly reduced. As mentioned above, the group of hypertensive patients who became normotensive during pregnancy account for a fair percentage of cases of postpartum hypertension.

5. (*a*) Cosgrove, S., and Chesley, L.: Management and Treatment of Late Toxemias of Pregnancy, Am. J. Obst. & Gynec. **51**: 67-74, 1946. (*b*) Chesley, L.; Somers, W., and Vann, F.: Further Follow-Up Study of Eclampsia, ibid. **56**: 409-421, 1948.

6. Teel, and Reid.[4] Reid, D. E., and Teel, H. M.: Nonconvulsive Pregnancy Toxemias: Their Relationship to Chronic Vascular and Renal Disease, Am. J. Obst. & Gynec. **37**: 886-896, 1939.

There is still the group of patients, however, whose blood pressure and optic fundi are normal throughout pregnancy, delivery, and the puerperium, but who, when seen at the sixth postpartum week, have an elevated blood pressure reading. By three months post partum, the blood pressure of most of these patients has returned to normal, and by six months post partum all have normal pressure. Stout,[7] Meyer and Nadler,[8] and Dieckmann [3] have reported this phenomenon. No explanation has been given. Is this the beginning of hypertensive vascular disease in these patients? Only long-term follow-up studies will answer this question.

TRUE TOXEMIA

The diagnosis for 45 patients was true toxemia. This was characterized by a rise in diastolic blood pressure and/or edema, and/or albuminuria, and the sign par excellence, a generalized retinal sheen (a wet, glistening appearance of the entire fundus). Since true toxemia is found most frequently in the young primigravid, we followed all young primigravid patients (less than 17 years old) at weekly intervals after their first prenatal visit, throughout the remainder of their pregnancy, and then at the usual three weeks, six weeks, three months, and six months post partum.

All of our 45 patients with true toxemia were under 20 years of age, except one. Their ages ranged between 13 and 22 years, with an average age of 17.5 years. No abnormalities were seen during the first six months of gestation. The arterial blood pressure remained normal, there was no abnormal weight gain, no edema, no albuminuria, and examination of the optic fundi showed them to be consistently normal. Sometime between six and one-half and eight and one-half months a generalized retinal sheen developed, though the blood pressure remained normal and no manifest signs of toxemia were present (no edema nor albuminuria). At seven and one-half months, the arterial blood pressure, particularly the diastolic pressure, increased (from 60 to 80 mm. Hg or from 70 to 90 mm. Hg), edema and albuminuria made their appearance, and the retinal sheen became more prominent. At term, or before if induction of labor was deemed advisable, the full-blown picture of toxemia was present, with an elevated diastolic pressure, facial and peripheral edema, albuminuria, and a prominent retinal sheen.

At three weeks post partum the arterial pressure was usually falling, edema had disappeared, a trace of albuminuria was usually present, and the retinal sheen, though still present, was diminished. At six weeks post partum, 25 patients had no symptoms and showed no signs or residuals of toxemia. The blood pressure was normal, edema and albuminuria were absent, and the retinal sheen had disappeared. In 20 patients, however, though the blood pressure had returned to normal and the manifest signs and symptoms of toxemia had disappeared, examination of the retinas revealed that the retinal sheen was now replaced by definite grade 1 or grade 2 retinopathy. Six of these patients have now been followed for 12 months. The retinopathy has remained unchanged although the blood pressure has continued to be normal.

Although the diagnostic and prognostic value of the ophthalmoscopic examination has been well established in hypertensive vascular disease, little has been written about the funduscopic findings in true toxemia of pregnancy. In true toxemia, the retinal vessels are entirely normal with the exception of segmental vasospasm. There is no increase in the arterial stripe, no tortuosity, and no arteriovenous nicking. Though the vessels are normal, the entire retina has a wet, glistening appearance; it seems to be covered by a thin film of fluid. This retinal sheen, because of its fluid nature, causes many reflections of light when the ophthalmoscope is focused on the fundus. The examiner, therefore, has difficulty in clearly outlining the retinal vessels; the more pronounced the sheen, the greater the difficulty. The many reflections of lights on a wet street at night resemble this phenomenon.

The retinal sheen is not a specific finding for toxemia of pregnancy, for it is also seen in acute nephritis (which simulates toxemia more closely than any other disease), the nephrotic phase of glomerulonephritis, and, to a much less degree, may occasionally be seen normally. In the normal patient, however, the wetness is localized and is never generalized. The real importance of this finding is that it is not seen in hypertensive vascular disease, and in our experience it has always been present in true toxemia. Just as papilledema is the best sign of malignant hypertension, although not restricted to that disorder, so a retinal sheen is the best sign of toxemia of pregnancy. The significance of this phenomenon is not known, but it probably represents superficial retinal edema, a consequence of the generalized vasospasm characteristic of toxemia. As the toxemia increases in severity, the retinal sheen becomes more obvious, and as the toxemia subsides the retinal sheen disappears.

In presenting our diagnostic criteria for true toxemia, it should be noted that the phrase "a rising diastolic blood pressure" is employed rather than a specific level of diastolic pressure. Although the conventional 140/90 mm. Hg may well be the upper limit of normality for the group of women 25 to 35 years old, a diastolic pressure of 90 mm. Hg is certainly abnormal for the majority of women under 20 years of age. In our experience, the average diastolic blood pressure in the group under 20 is 60 to 70 mm. Hg at three to four months gestation, and the pressure remains at this level if the pregnancy is uncomplicated. It is apparent, therefore, that a rise in diastolic pressure from 60 to 80 mm. Hg or from 70 to 90 mm. Hg is very significant in an individual patient and represents an abnormal blood pressure elevation. The cases of eclampsia reported as occurring with a normal blood pressure undoubtedly fall into this category.

A patient with postpartum eclampsia that occurred on the fifth postpartum day deserves special mention in this regard. From the third to the seventh month of pregnancy, her arterial pressure was 110/60 mm. Hg with no signs or symptoms of toxemia. At term her arterial pressure had risen to 120/80, and 2 + albuminuria and slight periorbital edema were present. Delivery was un-

7. Stout, M. L.: Hypertension 6 Weeks Postpartum in Apparently Normal Patients, Am. J. Obst. & Gynec. **27**: 730-733, 1934.

8. Meyer, H., and Nadler, S. B.: Unexpected Post-Partum Hypertension, Am. J. Obst. & Gynec. **41**: 231-236, 1941.

eventful. During the first four postpartum days, the average blood pressure was 120/90; periorbital edema and albuminuria persisted. On the fifth postpartum day, two generalized convulsions occurred. This patient's postpartum course was falsely considered to be benign because of the "normal" blood pressure recordings, and therefore no hypotensive measures were employed. The persistence of the 90 mm. Hg diastolic pressure was a 30 mm. Hg elevation of this girl's usual diastolic pressure.

COMMENT

Whether toxemia causes permanent vascular damage is a point that has been debated with much confusion. The main reason for confusion, as Dieckmann has said, has been a mistaken diagnosis during pregnancy, for example, a diagnosis of toxemia when hypertensive vascular disease was actually present.[3] That this error in diagnosis is common is readily seen by the fact that although 95% of the patients sent to our clinic were originally given a diagnosis of toxemia, by our criteria only 14% actually had toxemia.

We believe that differentiation between true toxemia and hypertensive vascular disease is readily apparent by examination of the retinas. Regardless of the age, parity, blood pressure level, pulse pressure, degree of edema, or albuminuria, if a generalized retinal sheen is present and the retinal arteries are normal, true toxemia is present. If a retinal sheen is not present and hypertensive retinopathy is seen, hypertensive vascular disease exists. If both a retinal sheen and hypertensive vascular changes are present, toxemia is superimposed on hypertensive vascular disease. Finally, if neither a retinal sheen nor hypertensive retinopathy is seen, and the arterial blood pressure is elevated, early hypertensive vascular disease is present.

Unless an accurate diagnosis is made originally, follow-up studies are obviously worthless. Furthermore, it is incorrect without serial studies to attribute hypertension, retinal changes, or renal impairment to a toxemic pregnancy that occurred five or more years previously. How then can one attribute vascular damage to toxemia of pregnancy? The finding of definite retinopathy in 20 of our 45 toxemia patients at six weeks post partum, whose retinas were entirely normal, prior to the toxemic episode, certainly suggests cause and effect. In these 20 patients the following sequence of events was seen: (1) normal blood pressure with normal fundi and no manifest signs of toxemia at three months gestation; (2) elevated blood pressure with a generalized retinal sheen, edema, and albuminuria at the height of toxemia; and (3) normal blood pressure, definite retinopathy, and no manifest signs of toxemia at six weeks post partum. These patients now have vascular disease without hypertension or any obvious renal impairment.

In our experience these retinal changes have been permanent. If these patients become pregnant again, they enter pregnancy with retinopathy. If the arterial pressure becomes elevated with a subsequent pregnancy and no retinal sheen develops, the disease is hypertensive vascular disease, not toxemia. If in a subsequent pregnancy a retinal sheen should return, toxemia is then superimposed on hypertension. The important consideration is that, once these retinal changes have developed, the patient will not have a pure toxemia again. She will either go through a completely normal pregnancy as hypertensive patients commonly do, or her hypertension will be aggravated by pregnancy as occasionally occurs, or toxemia will be superimposed on chronic hypertension.

Why in 20 patients with true toxemia retinal changes developed and in 25 these changes did not develop is unknown. It is illogical to think that there are two types of preeclampsia-eclampsia, indistinguishable clinically, one causing vascular damage, the other not. Severity of toxemia does not seem to be the deciding factor in determining if vascular damage is to follow, for, if this were so, a much higher incidence of vascular damage would be seen after eclampsia. Page and Cox,[9] Dieckmann,[3] and Chesley [5b] have found that toxemias without convulsions are associated with a higher incidence of permanent vascular-renal damage than actual eclampsia. Retinal examination in seven of our nine patients with eclampsia was normal at six weeks post partum.

Experience in our clinic coincides with that of Gibberd,[10] Peckham,[11] Chesley,[5b] and others [3] who maintain that the longer the duration of the first toxemia the greater the incidence of vascular damage. The average duration of the toxemic process (uncontrolled by therapy) in the group that ultimately showed retinal changes was 6.2 weeks; the average duration of toxemia in the other group was 2.4 weeks. Undoubtedly the reason that so many patients who have eclampsia escape vascular damage is that they are treated promptly and intensively.

Though the theory is certainly unproved, it is attractive to hypothesize that the generalized vasoconstriction, characteristic of toxemia and most readily determined by funduscopic examination, if allowed to continue beyond a critical period (more than one month), causes definite vascular damage. At first, the only residual evidence of this vasoconstriction may be retinopathy; the arterial blood pressure may be normal. It is at this stage that these patients are seen from the sixth week to the first year post partum.

SUMMARY

Examination of the retinas will permit differentiation between pure toxemia of pregnancy and hypertensive vascular disease. The 303 patients studied had hypertensive vascular disease, hypertensive vascular disease plus superimposed toxemia, postpartum hypertension, or true toxemia. Ninety-five per cent of these patients were referred to our clinic by the obstetricians with a diagnosis of true toxemia. Though 149 of the hypertensive group remained hypertensive during pregnancy, 67 patients became normotensive during pregnancy and became hypertensive again immediately after delivery. Two

9. Page, E. W., and Cox, A. J., Jr.: Renal Changes Following Toxemias of Late Pregnancy, West. J. Surg. **46**: 463-479, 1939.

10. Gibberd, G. F.: Albuminuria Complicating Pregnancy, Lancet **2**: 520-526, 1931; Significance of Recurrence in Late Toxemias of Pregnancy, J. Obst. & Gynaec. Brit. Emp. **41**: 23-34, 1934.

11. Peckham, C. H., Jr.: Time of Onset and Duration of Toxemia of Late Pregnancy in Relation to Development of Permanent Vascular Damage, Am. J. Obst. & Gynec. **42**: 638-645, 1941.

patients in the group who had hypertensive vascular disease plus superimposed toxemia, and showed grade 1 hypertensive retinopathy prior to the toxemic episode, showed grade 2 retinopathy six weeks post partum. All the patients with true toxemia showed a generalized retinal sheen, a wet, glistening appearance of the retinas. Though not a specific finding for toxemia, its importance lies in the fact that it is not seen in uncomplicated hypertensive vascular disease. Examination of the retinas in 25 of the true toxemic group six weeks post partum revealed no abnormality. In 20 patients, however, despite return of the blood pressure to normal and disappearance of edema and albuminuria, examination of the retinas revealed definite retinopathy. These retinal changes are attributed to the duration of the toxemia rather than to its severity.

PROLONGED HYPOTENSIVE REACTION TO HEXAMETHONIUM

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Recently hexamethonium compounds have been widely utilized in this country for the therapy of hypertension. Hexamethonium compounds are anticholinergic drugs that block sympathetic and parasympathetic ganglions of the autonomic nervous system. Side-effects from these compounds are a result of parasympatholytic effects resulting in obstipation, ileus, blurred vision, dryness of the mouth, and urinary retention, and sympatholytic effects resulting in severe hypotension with possible exacerbation or precipitation of cerebral, cardiac, or renal damage. The purpose of this report is to present three cases that will emphasize the prolonged hypotensive reaction that may result from the oral administration of hexamethonium compounds.

REPORT OF CASES

CASE 1.—A 48-year-old Negro woman was first seen at Charity Hospital outpatient department in April, 1952. A few days before, she had been seen in another department, with a chief complaint of weakness, visual blurring of three weeks' duration, and a history of hypertension for six years. She was referred to the medical outpatient clinic, at which studies revealed a blood pressure of 270/140 mm. Hg, moderate cardiac enlargement, marked impairment of renal function, and a moderate anemia. It was decided to start this patient on hexamethonium. She was advised to return promptly for weekly clinic visits and cautioned to discontinue therapy with the drug if any untoward symptoms developed. From April until October, 1952, the patient was treated in the outpatient department with hexamethonium. There was good control of blood pressure, most readings being 130/80 mm. Hg. Three weeks before admission the dose was increased to 500 mg. every six hours because of return of hypertension levels. She failed to return to the clinic and continued taking 500 mg. of hexamethonium every six hours. Beginning at that time the patient noted progressively increasing weakness and dizziness. Vomiting occurred seven days prior to admission. Urine output was noted to diminish beginning four days before admission, with anuria for the last 48 hours. During the last two days before admission the patient slept almost constantly and consumed only one to two glasses of water per day.

Physical examination revealed a very lethargic, extremely dehydrated woman. There was no evidence of head trauma. Blood pressure was 80/50 mm. Hg, pulse rate was 56, and respirations, 20. Funduscopic examination revealed marked arteriolar spasm and auriculoventricular nicking, a few hemorrhages and exudates, and normal disks. The lungs were normal. The heart was enlarged to the anterior axillary line. A harsh systolic murmur was audible both at the apex and base. Abdominal examination revealed no abnormalities. Neurological examination, except for the sensorium, was essentially normal. No localizing signs were obtained.

Laboratory studies revealed 5.5 gm. per 100 cc. of hemoglobin (Sahli method), volume of packed red cells, 20%; and 1,550,000 red blood cells per cubic millimeter. Urinalysis revealed a specific gravity of 1.006, a trace of albumin, no sugar, 5 to 8 leukocytes and 3 to 5 erythrocytes per high power field. Venous pressure was 180 mm. H_2O. Blood serology findings were normal. Blood urea nitrogen was 120 mg. per 100 cc., and blood creatinine was 25.4 mg. per 100 cc. The carbon dioxide combining power was 9 mEq. per liter, and the serum chloride level was 85 mEq. per liter. The electrocardiogram was compatible with left ventricular hypertrophy and lateral myocardial ischemia. Because of the marked hypotension and oliguria, arterenol therapy was begun as a continuous intravenous drip, on admission. Administration was required for four days because of the prompt return of the blood pressure to shock levels when therapy was stopped briefly. The urine output began to increase on the second day and was normal by the fourth day, at which time the use of arterenol was discontinued. Blood pressure failed to rise to its previous high levels but remained between 130/80 and 150/90. A repeat electrocardiogram taken nine days after admission showed a disappearance of the ischemic pattern seen on admission. Repeated urinalyses showed 2 to 20 red blood cells. The anemia failed to improve during the two month period of hospitalization despite transfusion of 2,000 cc. of blood. The blood urea nitrogen slowly fell to 60 mg. and the creatinine to 9.9 mg. at the time of discharge on the 59th hospital day.

CASE 2.—A white man, aged 60 years, had received therapy for hypertension since 1948. His blood pressure recordings over the past six years ranged from 210 to 280 mm. Hg systolic and 110 to 140 mm. Hg diastolic. There had been no episodes of congestive failure and no clinical or laboratory evidence of impaired renal function. He occasionally had attacks of supraventricular tachycardia that were terminated by rapid intravenous digitalization with lanatoside C. In June, 1952, paroxysmal headaches developed that increased in intensity and frequency and were associated with blood pressure elevations to levels of 260 systolic and 140 diastolic during the next four weeks. The results of urinalysis, hematological studies, amount of blood nonprotein nitrogen, and renal function tests were within normal limits at this time. His electrocardiogram was compatible with left ventricular hypertrophy. Hexamethonium therapy was started in July, 1952, with gradually increasing doses. Initially he received 250 mg. four times daily. Therapy was continued for 16 days with a reduction in blood pressure to 168/110 and without side-effects. His dosage at this time was 500 mg. twice daily and 250 mg. twice daily. He complained of failure to have a bowel movement for 24 hours and was given an enema on the 16th day of therapy. He awakened on the 17th day of hexamethonium therapy complaining of weakness and nausea.

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He became "cold and clammy" and was admitted to the hospital where his blood pressure could not be obtained. Incision and cannulation of a vein was performed, and an infusion containing arterenol was required to maintain a normal blood pressure. Whenever the infusion was discontinued, the patient's blood pressure would fall to shock levels. During this period repeated electrocardiograms failed to reveal any QRS changes to suggest myocardial infarction. Urinary output was maintained at a normal level, and there was no rise in blood nonprotein nitrogen. The patient was discharged with a blood pressure of 190/120 mm. Hg.

CASE 3.—A white man, 52 years old, was first seen on Sept. 10, 1952, complaining of "mild headaches and high blood pressure." After recovery from a subdural hematoma four years previously, an elevated blood pressure was noted for the first time. The patient remained asymptomatic until 1950, when severe substernal pain was experienced, and an electrocardiogram at that time was compatible with posterior myocardial infarction. The patient was hospitalized for three weeks and made an uneventful recovery. At that time his blood pressure was noted to be 180/110 mm. Hg. The patient began to notice mild headaches four months previous to his September admission. He had no evidence of heart failure in September, 1952. Physical examination at that time revealed blood pressure of 230/130; there were grade 2 eyeground changes. The heart was slightly enlarged to percussion. There was a diastolic gallop. The femoral pulses were bounding. The urine showed a trace of albumin and no formed elements in the sediment. Fluoroscopy revealed slight left ventricular enlargement and a dilated tortuous aorta. The electrocardiogram was compatible with left ventricular hypertrophy, anterior lateral myocardial ischemia, and possible healed posterior myocardial infarction. The nonprotein nitrogen measured 40 mg. per 100 cc., and 45% of phenolsulfonphthalein was excreted in the first hour, 15% in the second hour. Therapy with 20 craw units of veratrum viride (Vertavis) three times daily was started in September, 1952.

In November, 1952, the patient began to complain of occasional attacks of nocturnal dyspnea. The blood pressure was unchanged. Examination revealed an early, high-pitched, diastolic aortic murmur. On Dec. 20, the patient was given hexamethonium chloride, 125 mg. every six hours. He was digitalized and given a mercurial diuretic. He improved considerably in the ensuing week. The doses of hexamethonium chloride were gradually increased to 875 mg. every six hours. By Jan. 3, 1953, the blood pressure had decreased to 160/100 supine and 140/80 erect, three and one-half hours after 875 mg. dose. On Jan. 16, the pressure was 148/90 supine, and 120/78 erect. At this time the dose was reduced by 875 mg. twice daily and 125 mg. twice daily. On Jan. 24, digitalis therapy was stopped. The urine contained no albumin. Phenolsulfonphthalein excretion rate was unchanged, and the nonprotein nitrogen was 40 mg. per 100 cc. The aortic diastolic murmur was no longer heard. On Feb. 5, the patient complained of a weak spell lasting 15 minutes, two and one-half hours after an 875 mg. dose. The dose was reduced to 625 mg. twice daily with 125 mg. twice daily.

The patient remained asymptomatic, conducting his usual duties until March 6, 1953, when he suddenly fainted at work and was brought to the emergency room of the hospital. The blood pressure was not then obtainable. An electrocardiogram showed posterolateral myocardial ischemia but no QRS changes to suggest recent myocardial infarction. The patient was given 2 cc. of 1% phenylephrine (Neo-Synephrine) hydrochloride intravenously and 20 mg. of ephedrine intramuscularly every two hours. The blood pressure rose quickly to 120/80 when taken with the patient supine but was not obtainable when he sat up. The electrocardiographic evidence of posterolateral myocardial ischemia disappeared in approximately 20 minutes. He received 20 mg. of ephedrine sulfate intramuscularly every two hours. He was rapidly digitalized. He received 15 mg. of mephentermine (Kyamine) whenever the blood pressure fell below 100 systolic. The urinary output was good, and the nonprotein nitrogen level remained unchanged. He was kept in bed in the hospital until March 16. At this time the blood pressure was 130/85 supine, 110/60 sitting up. By March 20, the blood pressure was 120/80 supine, 110/80 sitting up, and 60/20 standing. By March 28, the blood pressure was 150/100 supine and sitting and 150/95 standing. All medication was stopped at this time. A retrograde pyelogram done on April 1, 1953, revealed marked deformity of the superior portion of the right caliceal system, which was displaced downward. The middle and inferior calices were normal. On April 10, a nephrectomy was done on the right kidney, and a large solitary cyst was removed. The patient made an uneventful recovery and was asymptomatic when discharged on April 20, 1953, with a blood pressure of 180/110 on standing.

COMMENT

There are three mechanisms that might result in a hypotensive reaction due to orally administered hexamethonium: (1) increased degree of absorption, (2) decreased renal excretion, and (3) excessive dosage. When normal intestinal function is present, only 10% of the orally administered drug is absorbed; the fraction absorbed is excreted almost entirely by glomerular filtration. An increase in the amount of hexamethonium absorbed may occur as a result of constipation, and this may contribute to the initial hypotensive reaction. The prolonged hypotensive reaction following discontinuance of hexamethonium would result from continued absorption of the drug that had accumulated in the intestinal tract as a result of decreased intestinal motility. Constipation would tend to be perpetuated by continuing effects of the absorbed hexamethonium. This mechanism was responsible in part for the reaction in case 2. Increase in the amount of drug absorbed may also occur during compensation from congestive heart failure. As edema of the intestinal wall subsides, there will be an increase in the amount of hexamethonium absorbed.

Decreased renal excretion would tend to cause higher blood levels of hexamethonium. When a hypotensive reaction occurs following initial impairment of renal filtration, the fall in blood pressure would result in a further diminution in filtration. This mechanism was responsible in part for the reaction in cases 1 and 3. Excessive dosage may result from many factors. There is a marked variation in the effective oral dose not only from patient to patient but in the same patient from time to time. This is dependent in part on variable absorption and excretion as well as on individual variation in sensitivity to the drug. It is important to adjust the dosage of hexamethonium according to the patient's blood pressure response in the standing position. It is essential in the proper management of patients who are taking hexamethonium that proper emphasis be placed on repeated regular medical care, report of any untoward symptoms, and discontinuance of therapy with the drug if any symptoms suggesting marked hypotension appear or if constipation occurs. The first case emphasizes the necessity of taking into consideration the patient's ability to cooperate and follow instructions carefully when receiving hexamethonium therapy.

SUMMARY

Reports of three patients with prolonged hypotensive reactions to hexamethonium are presented. The contributions of increased absorption, decreased excretion, and excessive dosage in the genesis of the hypotensive reaction are discussed.

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SYNDROME OF EPISODES OF HYPERSOMNIA, BULIMIA, AND ABNORMAL MENTAL STATES

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The episodic occurrence of states of excessive hunger (bulimia) and excessive sleep (hypersomnia) has been referred to as the Kleine-Levin syndrome by Critchley and Hoffman,[1] by Ronald,[2] and also by Palmer.[3] In Kleine's [4] series of five cases only two fit the syndrome to which his name later became attached, and it remains the merit of Levin [5] to have clearly recognized the peculiar syndrome of "periodic somnolence and morbid hunger." Many of the case histories described in the literature (Kaplinskiy and Schulmann,[6] Levin,[5] Critchley and Hoffman,[1] Ronald,[2] and Palmer [3]) indicate that periodic somnolence and excessive hunger are not the only two features of the syndrome and that psychopathological phenomena should be added as the third component of the syndrome. Recent observers [7] expressed the belief that the syndrome was confined to the male sex and the younger age group with onset in the second decade. The purpose of this article is to report three cases observed recently at the Neurological Institute of Presbyterian Hospital in New York.

REPORT OF CASES

Case 1.—A 58-year-old married white woman suffered at the age of 46 an acute episode of diarrhea, while temporarily living in Haiti. Complete examination, including the routine laboratory tests, revealed no abnormalities. At the termination of the intestinal episode, the patient entered into a period of somnolence and hypersomnia associated with depression, fatigue, extreme hunger, weakness, and frequent yawning, which lasted about three weeks. Similar episodes have continued to occur about two to three times a year since then. The longest free interval was six months and the shortest two months. Prior to being seen by us, the patient had two very thorough hospital studies in a teaching hospital in New York, which failed to reveal any plausible explanation for these episodes. On one occasion mild hypoglycemia was found, and the existence of mucous colitis was assumed. On repeated examinations the hypoglycemia could not be confirmed. Coarsened gastric rugae and mild hypertension were the only abnormal findings at the second hospital admission. The patient was considered to be suffering from a psychoneurosis with anxiety and had received dynamically oriented psychotherapy.

When the patient came under our observation in August, 1951, the pattern of the individual episodes was fairly identical, although there was some variation in the severity of the various symptoms. At the onset of an attack the patient noticed a bluish discoloration of her extremities, which were cold and showed almost permanent goose flesh. During this period, which might last several days to two weeks, there was excessive hunger. The patient would consume several times the amount of her normal food intake. While she had a special craving for sweets, she would eat anything available. On one occasion she consumed six thick slices of bread and two portions of ice cream between meals. Normally she was a very moderate eater. This first stage was usually terminated by a violent bout of diarrhea and occasional vomiting. The second stage was characterized by excessive malaise, fatigue, weakness, and hypersomnia. The patient would sleep for most of the day and night. When awakened, her speech was slow, there was slowness of thought, and all motor activity was considerably reduced. She appeared to be apathetic and drowsy, but whenever awake, was voraciously hungry. She always awoke to urinate and move her bowels and was never incontinent. The minimal amount of sleep daily during this stage was 18 out of the 24 hours. The remaining hours were spent in a state of apathetic somnolence, during which she could hear and understand but felt far away and remained entirely indifferent to her environment. She yawned frequently, the fingers were cyanotic, and the extremities were cold. When awake the patient, in addition to the aforementioned symptoms and complaints, had various complaints like backaches, tenesmus, epigastric pains, eructations, itching of the vagina, and palpitations. The duration of this period of hypersomnia and somnolence associated with bulimia was four to five days. During this state the patient ran a low-grade fever of about 100 F. The patient usually had an almost complete amnesia for the events occurring during this episode. When emerging from this second stage the patient became profoundly depressed and wept often, showing the cardinal symptoms of a true depressive psychosis, with melancholia, inhibition of will power, retardation of the stream of thought, and sense of worthlessness. On several occasions there was a true depressive stupor with mutism, and on other occasions the patient exhibited suicidal tendencies during this depressive stage. Normally this patient was of syntonic temperament, extroverted, "happy-go-lucky," with manifold interests and activities and a warm relationship to her husband and other members of her family. The duration of the depressive stage was one to four weeks. At the end of the depressive episode the patient resumed her normal appearance, temperament, behavior, and activities. It is noteworthy that the hyperphagia never resulted in any gain in weight.

It was impossible to hospitalize the patient during one of the episodes. When she was admitted to the Neurological Institute of the Columbia-Presbyterian Medical Center, on April 3, 1952, the patient was of slight body build and looked her stated age of 58 years. The findings on general and neurological physical examination were not remarkable except for a blood pressure of 150/90 mm. Hg, a fibroid tumor of the uterus and pyorrhea.

Neurological examination revealed no abnormalities. The laboratory findings were completely normal except for a sedimentation rate of 34 mm. per hour. Blood sugar and insulin tolerance curve were within normal limits. On repeated examinations the urine contained no porphyrin. Her skull roentgenogram revealed no abnormalities except calcification in the internal carotid arteries. The electrocardiogram was reported as showing normal function. A gastrointestinal series showed distortion of the mucosal folds on the greater curvature of the stomach, probably owing to hypertrophic gastritis. The electroencephalogram was normal on two occasions. These records were taken after the patient had already emerged from the state of hypersomnia, somnolence and bulimia, although she was still in the depressive third stage.

Case 2.—The second patient was a 34-year-old man who since the age of 17 had experienced episodes of excessive sleep —18 to 20 hours a day—at intervals of about six months.

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Read in abstract form before the Fifth International Neurological Congress in Lisbon, Portugal, Sept. 11, 1953.

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When awake, he drank about 10 cups of water and ate large amounts of food, particularly sweets, for which he ordinarily had no craving. These episodes usually lasted from several days to about two weeks. During the period of hypersomnia, he invariably entered into a state of depression of variable duration, which sometimes lasted several months. The depression had all the characteristics of a true depressive psychosis, with melancholic affect, severe inhibition of will power and psychomotor activity, a sense of guilt, and suicidal tendencies. On one occasion he made a suicidal attempt. Physical examination and laboratory studies revealed nothing abnormal in this case. The patient when seen had been under psychoanalytic treatment for more than 10 years. The treatment had been undertaken in order to cure the condition but had been entirely unsuccessful.

Case 3.—The third patient was a 16-year-old white youth who was studied at the Neurological Institute in April, 1953. At the age of 6 years he fell out of a tree, was semistuporous and was hospitalized. General examination and laboratory studies revealed no abnormalities except for the presence of a Babinski reflex on the right and loss of vision for a few hours after the accident. The patient made a quick recovery. When he was 10 years old, on a picnic it was noticed that the patient's body was covered with ticks. About one week later fever, vomiting, a stiff neck, and a short-lasting paralysis of the right leg developed. The spinal fluid was reported as normal. At the age of 14, following chickenpox, varicella encephalitis developed, with a fever and confusion of two days' duration. For about two months following the termination of the acute illness, he remained depressed and had poor coordination. He then became asymptomatic. About five months after the varicella encephalitis the first episode of hypersomnia occurred, during which he slept 16 to 18 hours a day and at the same time, while awake, consumed excessive amounts of food. During these episodes his eating habits were sloppy. While the patient recognized other persons, his memory and recall were extremely poor. He was interested in none of his usual occupations or friends, preferring to remain by himself and stated that "things seem cloudy and unreal." The duration of the entire episode was usually about one week, and the intervals were from three weeks to about four and a half months. In the free intervals the patient was completely normal.

The last episode, which led to the patient's hospitalization, was entirely different from his usual attacks. The night before its onset he was severely depressed and irritable. On the following morning he complained of sudden severe headache, nausea, vomiting, vertigo, inability to see on the right, paralysis of the right arm, inability to talk, and numbness of the right side of his face. His speech was thick and garbled, and he did not seem to understand what was being said to him. These symptoms lasted about an hour, following which he was completely normal except for a continuation of the severe headache. Then again he went into a clouded state not remarkably different from those in the past. The patient had a partial amnesia for what happened in the clouded states. This patient's general physical examination revealed nothing remarkable except for a temperature of 100 F. His neurological status was entirely normal. The electroencephalogram showed abnormal responses to hyperventilation. Synchronous bursts of high voltage at 3 per second activity were seen on many occasions, with bifrontal preponderance. Results of the remainder of the laboratory examinations, including routine studies of the blood and urine, blood chemistry, and cerebrospinal fluid were negative. Besides the routine studies, blood agglutinations for tularemia and brucellosis were negative, as were also studies for rickettsia. Psychometric studies and psychiatric investigation during the interval were noncontributory.

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COMMENT

It appears that all three patients have a syndrome characterized by the episodic occurrence of hypersomnia, somnolence, bulimia, and psychopathological manifestations. In all three cases the psychopathology contains the elements of clouded sensorium, partial or total amnesia for certain periods of the attack, and psychomotor retardation. In the first two cases, these phenomena are coupled with a severe affective derangement, a depression. In the first and third case, the presence of a low-grade fever could be ascertained. Polydipsia was present in the second case. The first patient presented numerous additional symptoms, such as acrocyanosis, goose flesh, and frequent yawning. In her case each episode could be clearly divided into three stages. The first stage consists of malaise, fatigue, and bulimia and is terminated by a gastrointestinal disturbance. The second stage consists of somnolence and chiefly hypersomnia. In the third stage a depressive psychosis exists. In the third case additional symptoms were in the form of visual, sensory, and motor disturbances. It is noteworthy that in two of the three cases the onset of the syndrome was preceded by an acute infectious illness.

In cases 1 and 2 there was very remarkable improvement after the patients were given a combination of *d*-amphetamine with small amounts of sodium amobarbital (Dexamyl). Both patients received the medication for a period of more than one year. No attempt at therapy was made in the third case. The first two patients have not experienced the triad of hypersomnia, bulimia, and mental disturbance to the same extent as before the treatment was started. The episodes continue to occur but at longer intervals and are much milder. They now present what may be called a *forme fruste* of the original syndrome. The first patient now experiences short episodes of somnolence and hypersomnia but not associated with bulimia and followed only by a very mild, sometimes almost unnoticeable, depression.

The indisputable response to an amphetamine drug, as well as many other features, suggests that this syndrome may be related to narcolepsy. Of course, the syndrome of hypersomnia, bulimia, and psychopathological manifestations is far from identical with narcolepsy. The onset of sleep does not have the acute imperative character of the narcoleptic sleep. Sleep does not occur under completely nonphysiological conditions as in narcolepsy. Its duration is entirely different, and there is no association with affective loss of tone. In common with narcoleptic sleep is its reversibility; in other words, the patient can be easily awakened. When asleep the patient gives the impression of sleeping naturally. On account of the abdominal and various autonomic features, one could think of a relation of the described syndrome to paroxysmal abdominal pain, observed as a form of epilepsy (Hoefer [8]) but the normal electroencephalogram in our patients and the absence of paroxysmal features serves to eliminate a relationship to the group of convulsive disorders.

Any possibility of hyperinsulinism can be dismissed, since none of the criteria (Wilder [9]) necessary for this diagnosis are present: the fasting blood sugar has never

been less than 50 mg. per 100 cc. and attacks are not precipitated by fasting and are not improved by the administration of sugar. Kirschbaum [10] described cases of abnormal hunger mostly as a symptom of brain tumor of either frontal or hypothalamic localization. Any attempt to localize the triad of symptoms, hypersomnia, bulimia, and mental disturbances, is, in the absence of autopsy findings, necessarily speculative. The third case particularly contains features that may raise the question of a relation of this periodic syndrome to migraine.

Roughly, but only roughly, comparable syndromes have been produced experimentally in animals by frontal lesions, (Fulton, Jacobsen and Kennard,[11] Fulton,[12] Watts and Fulton,[13] Mettler,[14] as well as by hypothalamic lesions (Fulton,[12] Hetherington,[15] and Mettler [16]). It is conceivable that this syndrome may not be strictly localizable at all, in this way resembling the other periodic and ictic disorders. Onset after an infectious illness has been observed by other authors as well as by me. Extensive psychotherapy in this chiefly nonpsychogenic disorder is useless, and the patient can be relieved to a great extent by administration of *d*-amphetamine.

SUMMARY

The syndrome consisting of recurrent episodes of hypersomnia, somnolence, and bulimia, possibly in association with gastrointestinal and other autonomic disturbances, followed by a depressive or clouded state, has been observed in three patients. The syndrome is not confined to males, as postulated by previous investigators, and is not confined to the younger age group, as also postulated by previous investigators. The onset after an infectious illness and the response to *d*-amphetamine are noteworthy. The syndrome may be related to narcolepsy. Localization is speculative, but evidence in the literature serves to implicate the frontal lobes and/or hypothalamus. The syndrome should not be mistaken for psychoneurosis.

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Accidents in Anesthesia.—If we are to keep the accident rate in anesthesia down to a minimum, there must be a realization by all concerned with surgical work that the anaesthetist, apart from his essential and fundamental part in the surgical team, is a dealer in highly lethal drugs and intricate procedures, and that death and disaster are never far distant; that it is incumbent upon every other member of the team to exercise every care and to cooperate to the limit for the sake of the safety and welfare of the patient; and that constant vigilance and concentration are the duty of everyone connected with administration of the anaesthetic.—C. N. Paton, Accidents in Anaesthesia, *The Medical Journal of Australia*, May 23, 1953.

CLINICAL NOTES

PATHOGNOMONIC ABDOMINAL SIGN FOR MECKEL'S DIVERTICULITIS

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Acute Meckel's diverticulitis in the adult does not often present a serious problem. Although the correct preoperative diagnosis is rarely made,[1] it is not necessary for effective management. Usually the diagnosis of acute appendicitis is made, and this wrong diagnosis will stimulate the right surgical treatment as it does in many other rare abdominal diseases. The resulting mortality rate for these cases in the adult is therefore low, as the treatment of the diverticulum and its complications is simple and effective when early surgery is instituted. Likewise, a low mortality results from cases in which the diverticulum bleeds, for here also a stimulus for surgery is presented by the dramatic sign of copious hemorrhage from the rectum of a young person.

Unfortunately Meckel's diverticulitis, although uncommon at any age, is most frequent in an age group that is almost free of acute appendicitis. In a recent series [2] of cases of pediatric abdominal surgery, 2,070 cases of acute appendicitis are reported. Less than 3% of these occur in children who were under 2 years of age. In my observation of 948 appendectomies, only one instance of acute appendicitis in children under the age of 2 years was encountered. There is a significant contrast in the report by Gross [3] of 149 cases of Meckel's diverticulitis, with 45% of the cases occurring in infants and children under the age of 2 years. It is apparent then that the diagnosis of acute appendicitis, the most common stimulus for surgical exploration, is lacking in cases in this very young age group, and as a result the overall mortality from Meckel's diverticulitis varies from 9.3% [4] to an alarming 57%.[5] This death rate can only be lowered if the preoperative diagnosis of an acute surgical condition in the abdomen of the very young child is more often correct. This is a difficult problem to resolve, however, as the vagaries of abdominal pain in the 2-year-old child are many. In addition, gastrointestinal symptoms in this age group are most often reflex in nature and arise from many commoner nonsurgical diseases. The physician examining the young patient does not often consider the diagnosis of acute appendicitis, because the condition is so infrequent at this age. It is more unlikely that he will suspect the presence of the rare Meckel's diverticulitis. Thus the

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infection is left to weaken and perforate the thin wall of the intestinal sac that does not have the protection of an adult omentum, and general peritonitis with its attendant high mortality follows.

The most pertinent effective aids in accomplishing a more nearly correct diagnosis of Meckel's diverticulitis (and therefore earlier surgery and lowered mortality) continue to be (1) the suspicion of its presence, or (2) the observation and recognition of a cardinal sign (rectal hemorrhage in a child) indicating its presence. Accordingly, it is the purpose of this paper to report a vivid abdominal sign not previously described which, when present, is pathognomonic of an underlying inflamed Meckel's diverticulum.

REPORT OF A CASE

A 4-month-old baby boy was admitted to the Kadlec Hospital on Feb. 28, 1950, with high fever, abdominal distention, and cyanosis. He had been well until three days prior to admission when anorexia and irritability had commenced. The same evening "abdominal colic" was noted and irritability appeared to be relieved by a copious bowel movement. During the next two days crying and irritability became worse, and the visiting physician made a diagnosis of upper respiratory infection. Conservative treatment caused no improvement, and on the evening of admission, grunting respirations could be heard over the telephone by the physician and immediate admission to the hospital was advised. There had been no diarrhea, chills, or cough. There was no rash, hematuria, or rectal bleeding. On admission, the baby was in severe respiratory distress. There was extreme general pallor and cyanosis of the lips and fingernails. The skin was moist, cold, and limp. The abdomen was markedly distended and tympanitic, and no bowel sounds were heard. There were basal rales on auscultation, and the heart sounds were rapid and free of murmurs. No masses could be felt in the abdomen, and there was no response from the completely listless baby on abdominal palpation. Rectal examination showed a toneless sphincter and empty rectum.

The temperature was 103.4 F, the pulse rate was 140, and the respiration rate was 40. Examination of the blood showed a red cell count of 3,020,000 with a hemoglobin value of 8 gm. (Hayden-Hauser) and a white cell count of 13,800 with 73% neutrophils (47 stabs). The urine was normal. The baby was admitted to the pediatric service and immediate surgical consultation was requested. Abdominal examination showed a peculiar cherry-red cellulitis involving the umbilicus and its surrounding circumference for about 2 cm. This sign was in striking contrast to the pallor and cyanosis of the rest of the distended abdomen. The signs of a generalized peritonitis were unmistakable, and the involvement of the umbilicus brought to mind the frequent connection of a Meckel's diverticulum to this structure. Further questioning revealed that the umbilicus had been completely normal until about eight hours prior to admission when mild periumbilical redness had commenced. Accordingly, a diagnosis was made of severe Meckel's diverticulitis, with perforation and general peritonitis. A previously taken flat plate of the abdomen supported the diagnosis of peritonitis. Laparotomy was advised.

A right rectus-splitting incision was made in the abdomen, and the dilated loops of the small intestine protruded through the abdominal incision. A markedly inflamed Meckel's diverticulum was found in its usual location on the ileum. Its distal aspect was blunt but connected to the umbilicus by a stout fibrous cord. There was a large perforation (0.5 cm.) in the midaspect of the diverticulum. Through this perforation fluid feces still poured; murky yellow, fluid feces were seen throughout the abdominal cavity. The fibrous cord was doubly clamped and divided at its juncture to the abdominal wall. The diverticulum was then clamped obliquely and removed. The clamp at the ileum was oversutured with fine gastrointestinal chromic catgut, and this layer of sutures was inverted with fine interrupted silk sutures. The abdomen was closed in layers of chromic catgut following the intraperitoneal instillation of 100,000 units of penicillin, 250 mg. of sulfanilamide, and 300 mg. of streptomycin. The abdominal cavity was not drained. The time required for the operation was 35 minutes.

Immediately postoperatively a 200 cc. whole blood transfusion was given. Penicillin, 75,000 units, was given intramuscularly every three hours. Streptomycin, 250 mg., was given in the same three-hour routine. In addition, 6 mg. of polymyxin was injected intramuscularly every six hours.[6] The peritoneal culture subsequently showed Escherichia coli. Daily urinalysis showed no abnormalities. The baby was placed in an oxygen tent for two days and lactated Ringer's solution with hyaluronidase (Alidase) was given subcutaneously daily. Glucose water was given orally.

The temperature chart showed a spiked pattern daily for five days, but the convalescence was otherwise uneventful. On the second postoperative day a small yellow bowel movement occurred and the glucose water given by mouth was changed to a milk formula. The periumbilical redness had completely disappeared by the morning of the third postoperative day. The wound healed without infection, and the baby was allowed to go home on the 10th postoperative day.

COMMENT

The case reported above is of interest for three reasons: 1. As far as I can determine, this is the youngest patient to survive a ruptured Meckel's diverticulum with generalized peritonitis. 2. The early use of polymixin and three other antibiotics with no complications seemed to have great therapeutic value. 3. A new abdominal sign was observed that permitted an immediate, correct diagnosis.

The embryologic origin of Meckel's diverticulum points out its close association with the umbilicus. For this reason, the presence of an umbilical discharge or cyst usually calls to mind the presence of the underlying sac. In these conditions the abnormality is present from birth and presents no difficulty in diagnosis. The dangerous diverticula have no such apparent connection with the umbilicus, but in approximately 20% of these cases the fibrous cord that is formed by the atrophy of the vitelline duct at the 7 mm. stage and that connects the umbilicus and intestine is not subsequently absorbed.[7] It is in those cases alone that the sign discussed above is possible; therefore the sign is, unfortunately, rarely seen.

The Meckel's diverticulum always has an independent artery and vein supplying it,[8] and in instances where it is connected to another structure by a fibrous cord, the latter structure also contains the anatomic supply of vessels and lymphatics. The inflammation extends contiguously as in any other lymphangitis and cellulitis, and in the patient reported on the cellulitis extended into the abdominal wall, the umbilicus, and the periumbilical region and gave a striking sign indicative of the intra-abdominal disease. The reversal of this process is seen in the omphalitis that gives rise to a peritonitis.

The presence of this sign brings to mind the occasional occurrence of other rare conditions of the umbilicus, all of which can be quickly excluded in the differential diagnosis. An infected omphalocele, cyst of the umbilical cord, cyst of the navel, "weeping um-

6. The use of polymyxin was made possible by a research grant from Burroughs Wellcome & Company, Inc., through the courtesy of Dr. D. S. Searle, Medical Director.

7. Shallow, T. A.; Eger, S. A., and Wagner, F. B.: Scientific Exhibit: Meckel's Diverticulum, Post. Grad. Med. **10**: 310-316 (Oct.) 1951.

8. Penberthy, G. C., and Benson, C. D.: The Complications of Meckel's Diverticulum in Infants and Children, S. Clin. North America **28**: 1221-1231 (Oct.) 1948.

bilicus," persistent vitelline duct, patent urachus, and urachal cyst are all excluded by the history of a previously completely normal umbilicus. Cases of primary omphalitis are also no problem in differentiation as they occur as contaminations of the umbilical cord and are most often continuous from birth and not seen in infants over 2 or 3 weeks old.

750 Swift Blvd.

WATERMELON SOUND

DIAGNOSTIC SIGN IN HYPERPARATHYROIDISM

Frederick A. Fender, M.D., San Francisco

On April 7, 1952, I was asked to carry out a neurological survey on a woman who had lost the ability to walk. A creature of habit, I began the examination with percussion of her head. Instead of the high-pitched crack, as evoked from a normal adult skull, there emerged a booming, low-pitched note that reminded me of the sound made by tapping on a watermelon. It turned out that the patient had hyperparathyroidism; at operation a

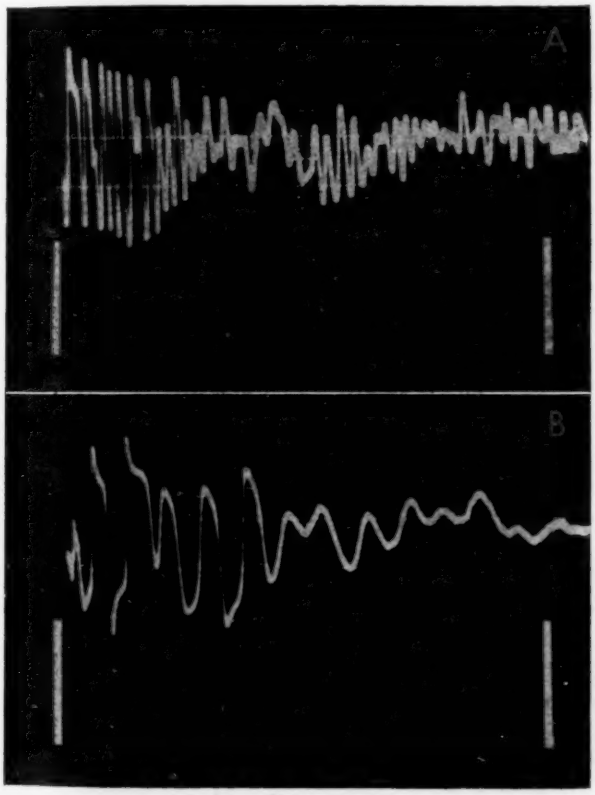

Fig. 1.—Oscillographic reproductions of the percussion notes of the skull of a normal adult, *A*, and the patient in case 3, *B*. Interval between the vertical markers is 20 milliseconds; the frequency of the abnormal note is approximately 800 a second.

parathyroid adenoma was removed. In succeeding months, two other patients with hyperparathyroidism were seen. Percussion notes were much the same in each instance. One patient whom I sought out, had Paget's disease and a skull with similar roentgenograms; this patient, however, had a normal-sounding skull. Sound recordings demonstrate clearly the difference between percussion notes of normal adult skulls and those of persons suffering from hyperparathyroidism (fig. 1). Tape recordings were made, in each instance, by placing a crystal type of Electrovoice microphone 1 cm. from the scalp. The percussion was carried out as close to the microphone as possible. A Magnacorder, type PT6AH, was used, with the tape traveling at 7.5 in. (19 cm.) per second.

Fig. 2.—Roentgenographic appearance of skull of patient in case 3.

REPORT OF CASES

CASE 1.—A 59-year-old white American housewife was admitted to St. Luke's Hospital on April 7, 1952, and seen in consultation that day. Her complaints were of inability to walk and pain in the back and right shoulder. Percussion of the skull evoked a low-pitched note. In addition to changes in the skull, generalized skeletal abnormalities were demonstrated roentgenologically. There was an old, ununited fracture of the right humerus. At operation on April 15, 1952, a spherical parathyroid adenoma, 2.5 cm. in diameter, was removed from the right lower pole of the thyroid.

CASE 2.—A 39-year-old white American salesman was admitted to St. Luke's Hospital on Oct. 1, 1952, with the chief complaint of pain in the legs and hips. There was a palpable nodule in the thyroid gland. There were widespread skeletal changes. The percussion note of the skull was low-pitched. At operation on Oct. 20, a spherical 3 cm. parathyroid adenoma was removed from the left lower pole of the thyroid gland.

CASE 3.—A 66-year-old white American woman was admitted to Stanford University Hospital on Jan. 26, 1953. The patient had children and was divorced. Her complaint was of generalized bone pains, referred chiefly to her back and lower extremities. She had sustained a pathological fracture of the humerus. Nodules were palpable in the thyroid gland. Studies of the bones, by roentgenogram (fig. 2) and by biopsy of the ulna, showed changes characteristic of hyperparathyroidism. In this instance also, a low-pitched, hollow-sounding note was elicited on percussion of the head.

The patient was operated on on Feb. 1, 1953. Three diffusely enlarged parathyroid glands were removed. These measured 2 by 3.5 by 6 cm., 1 by 2 by 6 cm., and 1 by 1.5 by 6 cm. and weighed 18, 4.1, and 1.8 gm., respectively. The pathologist's diagnosis was severe, multiple, diffuse parathyroid hyperplasia. It was of the clear cell type.

Associate Clinical Professor of Surgery (Neurosurgery), Stanford University School of Medicine, and Chief, Neurosurgery, St. Luke's Hospital.

The sounds were recorded by the Harry McCune Sound Service, and the photographs were made by Dr. Donald K. Reynolds, Senior Research Engineer, Stanford Research Institute.

Photographs of the oscillographic tracings were made with a Dumont oscillographic camera, no. 297, with Polaroid Land film and a lens aperture of f 1.9, was used. The oscilloscope was Tektronix, type 514-D. Prof. Henry S. Kaplan, Stanford University Hospital, Department of Radiology, made these cautious comments on the roentgenogram: "The calvaria are thickened, but unlike Paget's disease the tables are thin and the diploic layers are much wider than normal. There is a coarse mottling or stippling (best seen in cases 1 and 3). There are no localized areas of increased density as might be expected in Paget's disease and no transverse spiculation such as is seen in Mediterranean anemia [hereditary leptocytosis]. The appearance is strongly suggestive of hyperparathyroidism."

2209 Webster St. (15).

SPECIAL ARTICLE

EVALUATION OF GAMMA GLOBULIN IN PROPHYLAXIS OF PARALYTIC POLIOMYELITIS IN 1953

SUMMARY OF THE REPORT OF THE NATIONAL ADVISORY COMMITTEE FOR EVALUATION OF GAMMA GLOBULIN

During the summer of 1953, the Communicable Disease Center of the United States Public Health Service sponsored a national program for the evaluation of the efficacy of gamma globulin in the prophylaxis of paralytic poliomyelitis. Health departments in 41 states and 4 cities actively collaborated in the study. The program was planned and executed in accord with recommendations of a National Advisory Committee. The present report consists of a brief outline of the organization and plan of the study, a summary of the major findings, and the conclusions of the advisory committee. A full report of the study will be published elsewhere.

ORGANIZATION AND PLAN OF STUDY

The National Advisory Committee consisted of authorities in poliomyelitis research, state health officers, epidemiologists from states and large cities, and a physical therapist. While the members served as individuals, most of them had participated in various capacities during the planning of the procedures for the national allocation of gamma globulin during the spring of 1953. Similarly, all were active in the field, laboratory, or clinic in the study of poliomyelitis and the effects of gamma globulin during the summer of 1953.

In considering its mission, the committee recognized that a practical objective was the collection of sufficient quantitative data to determine, if possible, the relative advantages and disadvantages of the administration of gamma globulin to an entire age segment in an epidemic area (mass use) and its use in household associates of poliomyelitis patients (contact use). The committee considered the different viewpoints expressed during the winter and spring of 1953 in the committees and agencies that devised the allocation plan for apportioning the supply of gamma globulin between mass use and contact use.

The direct scientific evidence obtained during the field trials of 1951 and 1952 [1] suggested the value of mass use, at least when the gamma globulin is administered at a suitable time prior to expected illness, in specified communities experiencing intense epidemics. It was clear, however, that the successful measurement of any mass effect, in terms of paralytic cases prevented or modified, would depend directly on the degree of efficacy of gamma globulin, the intensity of the epidemic, and the time when inoculations were given in relation to the rise and fall in incidence of cases. There was some doubt whether the number of severe epidemics that would occur in the country would utilize effectively more than a small proportion of the anticipated supply. Furthermore, it was problematic whether the subsequent course of an epidemic in a threatened community could be predicted with sufficient accuracy and in sufficient time to permit the necessary community organization to inoculate the children at risk before the epidemic waned.

Answers to such questions could be obtained only from practical field experience. Therefore, one of the

This study was sponsored by the United States Department of Health, Education, and Welfare, United States Public Health Service, Communicable Disease Center, Atlanta, Ga., in collaboration with the Association of State and Territorial Health Officers, the American Physical Therapy Association, and the D. T. Watson School of Physiatrics, affiliated with the University of Pittsburgh School of Medicine.

The members of the National Advisory Committee for the Evaluation of Gamma Globulin are as follows: Lucy Blair, Consultant, Professional Services, American Physical Therapy Association, New York; John M. Chapman, Epidemiologist, Los Angeles City Health Department, Los Angeles; Roy F. Feemster, Director, Division of Communicable Diseases, Massachusetts Department of Public Health, Boston; Thomas Francis, Jr., Professor of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Mich.; D. G. Gill, State Health Officer, Alabama State Department of Health, Montgomery, Ala.; A. L. Gray, Director of Preventable Disease Control, Mississippi State Board of Health, Jackson, Miss.; Morris Greenberg, Director, Bureau of Preventable Diseases, New York City Health Department, New York; William McD. Hammon, Professor of Epidemiology, University of Pittsburgh School of Public Health, Pittsburgh; Arthur C. Hollister, Jr., Chief, Bureau of Acute Communicable Disease, California State Department of Public Health, Berkeley, Calif.; Robert F. Korns, Director, Bureau of Epidemiology and Communicable Disease Control, New York State Department of Health, Albany, N. Y.; John R. Paul, Professor of Preventive Medicine, Yale University School of Medicine, New Haven, Conn.; John D. Porterfield, Director of Health, Ohio Department of Health, Columbus, Ohio; Albert B. Sabin, Professor of Research Pediatrics, University of Cincinnati College of Medicine–Children's Hospital Research Foundation, Cincinnati; Leonard M. Schuman, Deputy Director for Division of Preventive Medicine, Illinois Department of Public Health, Springfield, Ill.; Thomas F. Sellers, State Health Officer, Georgia Department of Public Health, Atlanta, Ga.; Jessie Wright, Medical Director, D. T. Watson School of Physiatrics, affiliated with the University of Pittsburgh School of Medicine, Pittsburgh; Alexander D. Langmuir, Chairman, Chief, Epidemiology Branch, Communicable Disease Center, Atlanta, Ga.; and Abraham M. Lilienfeld, Secretary, Consultant to the Communicable Disease Center and Assistant Professor of Epidemiology, Johns Hopkins University, School of Hygiene and Public Health, Baltimore.

This study was conducted by the National Gamma Globulin Evaluation Center, Abraham M. Lilienfeld, Director, a temporary administrative unit organized within the Communicable Disease Center, Theodore J. Bauer, Medical Officer in Charge. Dr. Lilienfeld, a consultant to the Communicable Disease Center, devoted his full time to the program until Sept. 23, 1953, and then returned to Johns Hopkins University. He retained general supervision after this date. Dr. Heinz Eichenwald was Acting Director from Sept. 23, 1953, to the termination of the program.

1. (*a*) Hammon, W. McD.; Coriell, L. L., and Stokes, J., Jr.: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 1. Plan of Controlled Field Tests and Results of 1951 Pilot Study in Utah, J. A. M. A. **150**: 739 (Oct. 25) 1952. (*b*) Hammon, W. McD.; Coriell, L. L., and Stokes, J., Jr.: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 2. Conduct and Early Follow-up of 1952 Texas and Iowa-Nebraska Studies, ibid. **150**: 750 (Oct. 25) 1952. (*c*) Hammon, W. McD., and others: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 3. Preliminary Report of Results Based on Clinical Diagnoses, ibid. **150**: 757 (Oct. 25) 1952. (*d*) Hammon, W. McD.; Coriell, L. L.; Wherle, P. F., and Stokes, J., Jr.: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis, ibid. **151**: 1272 (April 11) 1953.

approaches considered for the evaluation program was to plan detailed epidemiological descriptions of each of the epidemics in areas where there was mass use.

With regard to the alternate method of use of gamma globulin, namely, contact use, no direct scientific evidence based on field observations was available to support its value. However, because household associates have an increased risk of developing poliomyelitis, it seemed likely that the administration of gamma globulin to these associates would equal, if not exceed, the benefits of mass use in terms of cases prevented or modified. The basis for these estimates, however, rested strongly on the assumption that gamma globulin administered within one week before onset would modify the severity of paralysis. This conclusion was reported by Hammon and associates, but the evidence was based on only 12 cases in his gamma globulin-inoculated group, compared with 16 cases in the gelatin-inoculated control group. Although the differences were statistically significant, conclusions based on such small numbers are hazardous in a disease as complex as poliomyelitis. There was a great need, therefore, to collect much more extensive data on the possible modifying effect of gamma globulin.

The committee recognized that it would be very difficult to conduct rigidly controlled studies in the United States during 1953. The committee recommended, therefore, that the effort be concentrated on the collection of a maximum amount of well-defined descriptive epidemiological data for careful analysis and comparison with the wealth of past epidemiological experience in this country. It was believed that a marked preventive effect of gamma globulin in the recommended dosages when given at the right time might be observed in large epidemics, even in the absence of rigid controls, in the form of consistent and repeated deviations from classical epidemiological patterns normally observed in the age group inoculated. If it had a marked modifying effect, this should be evident in the mildness of the paralysis among patients becoming ill with poliomyelitis after receiving gamma globulin. While recognizing certain difficulties in this plan of investigation, the committee nevertheless agreed that efforts should be made to collect the best possible data and to analyze them for valid conclusions.

Specifically, the committee recommended four approaches to the problem: (1) descriptive epidemiological studies for each of the areas where mass use of gamma globulin was employed; (2) comparison of the severity of paralysis of patients in whom the disease developed immediately before mass use with the severity of those acquiring the disease after receiving gamma globulin; (3) study of the severity of paralysis among multiple case households, namely, those households in which two or more cases of poliomyelitis were reported; and (4) documentation of administrative aspects of the distribution of gamma globulin.

The program followed the general plans and objectives established by the committee. In June an outline of the plans was sent to all state health officers with an invitation that they join in the undertaking. The response was immediate and enthusiastic. The population of the 41 states and 4 cities participating in the study constituted about 90% of the population of the whole country. Thus, the program was truly national in scope.

A National Evaluation Center with headquarters in Atlanta was organized as a special task force for the program. A group of 20 epidemic intelligence service officers, 8 nurse officer epidemiologists, and 6 statisticians was assigned by the Communicable Disease Center for essentially full-time duty in the program. A group of 38 physical therapists was mobilized by the American Physical Therapy Association.

Detailed epidemiological descriptions were collected in each of the 23 areas where mass inoculations of gamma globulin were given. In five of these areas the incidence of poliomyelitis after the gamma globulin administration was sufficiently great to warrant assigning a physical therapist for special studies to measure the possible modifying effect of gamma globulin.

The most extensive aspect of the program was the study of households from which more than one case of poliomyelitis was reported. In all participating states and cities record systems for matching case reports were organized either at the local or state level to identify multiple case households. As soon as possible after the identification, field visits were made to the hospital or the home to collect uniform data. A standard form was provided. The main purpose of this visit was to verify the diagnosis and to secure dates of onset that were as accurate as possible. Many different sources of data of varying completeness and accuracy were used. Special effort was made, however, to determine the status of paralysis during the period from 7 to 14 days after onset.

All reported patients in multiple case households were examined by a specially trained physical therapist 50 to 70 days after the onset, using a special abridged system of muscle grading that permitted an estimate of the extent of paralysis on the basis of muscle bulk involved. An index could be calculated and expressed in terms of percentage of muscle damage. Studies had shown that a rather high degree of consistency in the determination of percentage of muscle bulk involvement existed between different examiners. In general, the average difference between examiners was approximately 3%. Data from households with multiple cases were included in this study if dates of onset fell within the interval from approximately June 1 to Oct. 31. Reports of 830 multiple case households comprising 1,828 reported cases of poliomyelitis were forwarded to the National Evaluation Center in the study. Data on the administrative aspects of gamma globulin distribution and utilization in the field were collected.

EVALUATION OF MASS USE

During 1953 gamma globulin was given by mass inoculation in 23 communities in 13 separate states. In all but two areas, entire county units were included. In one instance mass inoculations were limited to a city and in another only portions of two adjacent counties were selected. The populations of these areas ranged from 6,800 to 139,000, with a majority falling in the 25,000 to 50,000 population group. The total number of children inoculated in these areas was close to 235,000.

In attempting to evaluate the efficacy of the mass use of gamma globulin, the descriptive epidemiological data collected in each of these areas were examined to see if consistent deviations from classic epidemic patterns were

discernible. According to the data of Hammon and associates, the preventive effect of gamma globulin should begin about one week after its administration and should persist at a significant level until about the fifth week. Since large scale poliomyelitis epidemics tend to occur in symmetrical form, mass inoculations, if administered at or before the peaks of epidemics, might be expected to produce consistent and observable drops in the epidemic curve beginning about one week later. An asymmetry in the epidemic curve might become apparent. This should be most marked in the epidemic curve limited to the inoculated age group.

Corollary effects might be observed. For example, a marked shift in the relative incidence of cases to older uninoculated age groups might occur beginning after the mass inoculations because of the reduced incidence expected in the age group receiving gamma globulin. Similarly, the duration of epidemics in the inoculated group might be modified. Furthermore, differences might be observed in paralytic attack rates within the inoculated age group according to whether or not gamma globulin had been given.

These effects are postulated on the following assumptions: (1) that the gamma globulin available in 1953 would be potent; (2) that the mass administration would be done at or before the peak of the epidemics; and (3) that the epidemics would be of sufficiently large scale. If, however, mass inoculations were given using less potent gamma globulin, or when the epidemics were already rapidly diminishing, or in small scale epidemics, then it would be difficult if not impossible to detect any effect attributable to gamma globulin. The results of tests performed by Youngner [2] on 6 lots of gamma globulin used by Hammon and his associates in 1952, and of Opton, Nagaki, and Melnick [3] on 65 lots used in 1953 indicate that the gamma globulin used in 1953 was generally not less potent than that used in the field trials of 1952.

A careful study of the 23 epidemics in which mass use of gamma globulin was employed in 1953 revealed that in 13 instances the epidemics were too small or the inoculations were given too late to permit further analysis. In the remaining 10 epidemics, however, comparisons were made for deviations from the classical epidemic patterns. A wide variety of asymmetrical epidemic curves was found and a comparison of these curves with those observed in epidemic areas this year where no gamma globulin had been employed revealed no consistent differences.

It was, therefore, concluded that asymmetry of epidemic curves could not be attributed with assurance to a gamma globulin effect and thus could not be utilized as a measure of the preventive action of gamma globulin on poliomyelitis, at least for outbreaks of the size studied in 1953.

A study of the age incidence following mass administration of gamma globulin revealed a shift to older uninoculated groups in many of the epidemics. An examination of available data based on present and past experience, however, revealed that these age shifts are quite variable and that similar shifts frequently occurred in areas where gamma globulin had not been used. The duration of the epidemics in mass inoculation areas was also compared with concurrent and past experience. Consistent differences were not found. Therefore, it was concluded that a study of neither the age shift nor the duration of the epidemic permitted valid conclusions regarding the effectiveness of mass use of gamma globulin in 1953.

Consideration was given to the possibility of comparing the paralytic rates before, during, and after the significant protection period described by Hammon and associates in the inoculated and uninoculated children of the same age group. It was noteworthy that many paralytic cases appeared in uninoculated children, considering the relatively small number of such children thought to exist. It was necessary, however, to question the validity of this comparison because of the presumably disparate composition and unknown size of the two groups. It was conceivable that factors existed that would make the uninoculated groups a biased selection. It was therefore improper to apply this method of analysis to the experience in counties where mass injections were given.

In the five counties where muscle gradings were performed 50 to 70 days after onset, 43 cases occurred in the eligible age group during the week immediately preceding the mass inoculations. A total of 48 cases developed after gamma globulin was given, 32 occurring from 1 to 7 days later and 16 from 8 to 31 days after. The severity of paralysis in these groups was compared. A modifying effect of gamma globulin was not statistically demonstrated.

Thus, while extensive and varied approaches were followed in the attempt to evaluate the efficacy of gamma globulin as used on a community inoculation basis in 1953, no valid basis was found for drawing confident conclusions as to its preventive effect. In order to resolve the questions concerning the efficacy of mass inoculation, further study with standardized material and proper controls would be required.

EVALUATION OF CONTACT USE

The primary purpose of the extensive study of multiple case households was to evaluate contact use of gamma globulin. Multiple cases of clinically diagnosed poliomyelitis occur in 3 to 5% of affected households. The interval between the first and subsequent cases has followed a rather characteristic pattern in many different epidemics. On the average, 60% of subsequent cases occur within 5 days after the first case, 30% in 6 to 12 days, and approximately 10% in 13 to 30 days. Gamma globulin was administered to familial associates of patients on the assumption that the resulting paralysis might be much milder in those in whom it would ordinarily develop within seven days of inoculation, while in a considerable proportion of the remainder paralysis might be completely prevented.

In 749 multiple case households, 1,654 individual cases of poliomyelitis were studied. Of this number, 749 were index cases, 8 were prior cases, 80 were co-index

2. Youngner, J. S.: Poliomyelitis Virus Antibody in Different Lots of Human Serum Gamma Globulin, Proc. Soc. Exper. Biol. & Med. **84**: 697 (Dec.) 1953.

3. Opton, E. M.; Nagaki, D., and Melnick, J.: Poliomyelitis Antibodies in Human Gamma Globulin, unpublished data.

cases, and 817 were recognized one or more days after the index case. For various reasons, depending mostly on the time required for recognition of the index case and the large proportion of secondary cases that develop simultaneously with or very shortly after the index case, about one-third of the patients in the subsequent cases received gamma globulin before the onset of their illness. To determine whether gamma globulin modified the severity of paralysis in these patients, the extent of muscle involvement in this group as well as in other groups of subsequent patients who either received no gamma globulin or received it on or after onset was carefully measured by specially trained physical therapists. For a number of reasons, fully outlined in the complete report, it was necessary to limit consideration to 415 subsequent patients who exhibited paralysis 50 to 70 days after onset of their illness. Of these 415 patients, 158 received gamma globulin before onset, 184 received no gamma globulin, and 73 received it on or after onset. The analysis based on the 50 to 70 day evaluation was regarded as more valid because it was found that only 8.6% of 338 patients for whom a diagnosis of paralytic poliomyelitis was made at 7 to 14 days after onset had insufficient paralysis at 50 to 70 days to warrant their inclusion, while 57% of 328 patients who at 7 to 14 days were classified as having the nonparalytic form or were only suspected of having nonparalytic poliomyelitis were found to be paralytic at 50 to 70 days. A statistical analysis showed no significant difference in the extent of muscle involvement in those who received gamma globulin before onset, as compared with those who received none or received it on the day of or after onset.

Another question investigated was whether the proportion of patients classified as having nonparalytic disease at 50 to 70 days in the group that received gamma globulin before onset was different from the proportion in the other groups mentioned above. No significant difference was found.

An analysis of the familial aggregation of all subsequent cases was made in order to obtain an indication as to whether the administration of gamma globulin may have prevented a considerable proportion of the cases that are expected to occur 13 to 30 days after the first case in the family. To permit comparison with the established pattern of previous years, it was necessary to include all the data obtained from multiple case households regardless of whether gamma globulin was given to any member of the family. When this was done, the pattern turned out to be similar to that observed in previous years when no gamma globulin was used.

There may be several alternative explanations for the apparent lack of effectiveness of gamma globulin in familial associates of patients with poliomyelitis: 1. Gamma globulin preparations may contain too little antibody to be effective in the dosage used. 2. Gamma globulin of adequate antibody content may be ineffective when it is given to patients after they have been infected, and the vast majority if not all familial associates of a patient may already be infected by the time the diagnosis is made in the first case or by the time inoculations can be given.

ADMINISTRATIVE ASPECTS

Administrative problems relating to the distribution of gamma globulin for inoculation of household associates within the states were fewer than expected after the material was received. The establishment, in advance, of definite criteria for its use helped to relieve pressure on practicing physicians and health departments. The evidence indicates that, once a request had been properly made, the globulin was provided promptly. The major delay centered around the interval between the onset in the index cases and the diagnosis; nevertheless, in several states from which data are available, gamma globulin was given to the great majority of household associates within an average of five days from the onset in the index cases. If gamma globulin is to be given earlier, it is apparent that efforts must be made to obtain earlier recognition of the first cases. On the other hand, the procedure for obtaining gamma globulin for mass use was necessarily involved. Because of the difficulty in making accurate predictions, the level of incidence required, and the need for approval of a request, the time required for the mass procedure was likely to delay administration until the peak was well past.

COMMENT

The mass use of gamma globulin carried out on a large scale in 1953 as a method to prevent paralysis in poliomyelitis infection was done as a public health measure in response to a widespread demand and not on an experimental basis. As such, attempts to draw conclusions regarding its efficacy have not been easy and in many instances impossible. In any event, the method of analysis of carefully compiled and extensive data on the use of gamma globulin in those epidemic areas and populations where it might have been expected to be effective did not yield statistically measurable results. Therefore, its value in community prophylaxis as practiced during 1953 has not been demonstrated. Nevertheless, the committee cannot say that the use of gamma globulin for this purpose produced no effect.

A serious difficulty encountered in arriving at conclusions about the results of mass use of gamma globulin in 1953 has been the lack of controls. Had such controls been available, the results would probably have been more clear cut and their evaluation easier. To obtain further data on the efficacy of mass use, further adequately controlled studies will be necessary.

On the other hand, the data on the efficacy of gamma globulin in contact use that have been accumulated in 1953 are considered to be adequate for reliable conclusions. They indicate that, with the preparations involved and in the dosages used, the administration of gamma globulin to familial associates of patients with poliomyelitis has had no significant influence on (1) the severity of paralysis developing in subsequent cases; (2) the proportion of nonparalytic poliomyelitis occurring in subsequent cases in which gamma globulin was given before the onset; and (3) the classic pattern of familial aggregation of cases in the country at large.

In view of these conclusions, the committee recommends that a careful reconsideration be given to the present procedures and methods of national gamma globulin distribution and utilization.

Comment by William McD. Hammon.—The data presented in this report deal with 23 small epidemics, in most of which gamma globulin was given far too late to be expected to have much or any effect. The data are not from an experiment set up with suitably chosen controls. In my opinion analysis of such data (as should have been expected beforehand and was by many) fails to demonstrate whether gamma globulin was or was not effective in the two types of usage to which it was put. It does show clearly, however, as I have attempted to predict previously,[4] that this agent has an extremely limited application in the field of preventive medicine and will not produce dramatic results in general use.

50 Seventh St., N.E., Atlanta, Ga. (Dr. Alexander D. Langmuir).

4. Hammon, W. McD.: Limitations in Use of Gamma Globulin in Poliomyelitis, Am. J. M. Sc. **226**: 125 (Aug.) 1953; Passive Immunization Against Poliomyelitis with Especial Consideration of the Effectiveness of Gamma Globulin, Bull. New York Acad. Med. **29**: 930 (Dec.) 1953. Hammon.[1d]

COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Acet-Dia-Mer-Sulfonamides (See New and Nonofficial Remedies 1953, p. 106).

The Bowman Bros. Drug Company, Canton, Ohio.

Tablets Cetazine: 0.5 gm. Each tablet contains 0.167 gm. each of sulfacetamide, sulfadiazine and sulfamerazine.

S. J. Tutag & Company, Detroit.

Suspension Buffonamide with Sodium Citrate: 473 cc. and 3.78 liter bottles. A suspension containing 33 mg. each of sulfacetamide, sulfadiazine, and sulfamerazine, and 0.1 gm. of sodium citrate in each cubic centimeter. Preserved with 0.75% methylparaben and 0.25% propylparaben.

Alkavervir (See New and Nonofficial Remedies 1953, p. 238).

Riker Laboratories, Inc., Los Angeles.

Tablets Veriloid: 1, 2, and 3 mg.

***p*-Aminosalicylic Acid** (See New and Nonofficial Remedies 1953, p. 89).

American Roland Corporation, New York.

Powder Para-Aminosalicylic Acid: Bulk; for manufacturing use.

Chlorotrianisene (See New and Nonofficial Remedies 1953, p. 366).

The Wm. S. Merrell Company, Cincinnati.

Oral Drops TACE: 30 cc. bottles. A flavored solution in vegetable oil containing 12 mg. of chlorotrianisene in each cubic centimeter.

Cyanocobalamin (See New and Nonofficial Remedies 1953, p. 486).

Standard Pharmaceutical Company, New York.

Solution Crystalline Vitamin B_{12} with Benzyl Alcohol 2%: 10 cc. vials. A saline solution containing 30 or 50 mcg. of cyanocobalamin in each cubic centimeter.

Estrone-U.S.P. (See New and Nonofficial Remedies 1953, p. 357).

Lincoln Laboratories, Inc., Decatur, Ill.

Solution Estrone in Oil with Benzyl Alcohol 2%: 10 cc. vials. A solution in sesame oil containing 0.5 mg. of estrone in each cubic centimeter.

Heparin Sodium-U.S.P. (See New and Nonofficial Remedies 1953, p. 222).

The Upjohn Company, Kalamazoo, Mich.

Solution Heparin Sodium: 1 cc. vials. A solution containing 20,000 U. S. P. units (approximately 200 mg.) of heparin sodium in each cubic centimeter. Preserved with 0.4% chlorobutanol.

The Vitarine Company, Inc., New York.

Solution Heparin Sodium: 10 cc. vials. A solution containing 1,000 U. S. P. units (approximately 10 mg.) or 5,000 U. S. P. units (approximately 50 mg.) of heparin sodium in each cubic centimeter.

4 cc. vials. A solution containing 10,000 U. S. P. units (approximately 100 mg.) of heparin sodium in each cubic centimeter. Preserved with 0.5% phenol.

Mercurophylline Sodium (See New and Nonofficial Remedies 1953, p. 305).

Chemo Puro Manufacturing Corporation, Long Island City, N. Y.

Powder Mercurophylline Sodium: Bulk; for manufacturing use.

Premo Pharmaceutical Laboratories, Inc., South Hackensack, N. J.

Solution Mercurophylline (Sodium): 2 cc. ampuls. A solution containing 140 mg. of mercurophylline sodium (equivalent to 39 mg. of mercury) in each cubic centimeter.

Sodium *p*-Aminosalicylate (See New and Nonofficial Remedies 1953, p. 91).

American Roland Corporation, New York.

Powder Sodium Para-Aminosalicylate: Bulk; for manufacturing use.

Tripelennamine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1953, p. 14).

Ciba Pharmaceutical Products, Inc., Summit, N. J.

Solution Pyribenzamine Hydrochloride: 1 cc. ampuls. A solution containing 25 mg. of tripelennamine hydrochloride in each cubic centimeter.

Tablets Pyribenzamine Hydrochloride: 25 mg.

Aminophylline-U.S.P. (See New and Nonofficial Remedies 1953, p. 309).

Rexall Drug Company, Los Angeles.

Tablets Aminophylline: 0.19 gm.

Amphetamine Sulfate-U.S.P. (See New and Nonofficial Remedies 1953, p. 187).

Lincoln Laboratories, Inc., Decatur, Ill.

Tablets Amphetamine Sulfate: 10 mg.

Ascorbic Acid-U.S.P. (See New and Nonofficial Remedies 1953, p. 502).

Standard Pharmaceutical Company, Inc., New York.

Tablets Ascorbic Acid: 25, 50, and 100 mg.

Bacitracin (See New and Nonofficial Remedies 1953, p. 45).

Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., Brooklyn.

Bacitracin (Parenteral): 50,000 unit vials.

Benzypyrinium Bromide (See New and Nonofficial Remedies 1953, p. 181).

Warner-Chilcott Laboratories, Division of Warner-Hudnut, Inc., New York.

Solution Stigmonene Bromide 1:500: 1 cc. ampuls. A buffered, saline solution containing 2 mg. of benzpyrinium bromide in each cubic centimeter.

Cortisone Acetate (See New and Nonofficial Remedies 1953, p. 346).

The Upjohn Company, Kalamazoo, Mich.

Tablets Cortisone Acetate: 5 and 10 mg.

Dia-Mer-Sulfonamides (See New and Nonofficial Remedies 1953, p. 108).

Physicians' Drug & Supply Company, Philadelphia.

Tablets Sulmeradine: 0.5 gm. Each tablet contains 0.25 gm. each of sulfadiazine and sulfamerazine.

Folic Acid-U.S.P. (See New and Nonofficial Remedies 1953, p. 487).

Rexall Drug Company, Los Angeles.

Tablets Folic Acid: 5 mg.

Hexamethonium Chloride (See New and Nonofficial Remedies 1953, p. 241).

Warner-Chilcott Laboratories, Division of Warner-Hudnut, Inc., New York.

Tablets Methium Chloride: 0.5 gm.

Hydrocortisone Acetate (See New and Nonofficial Remedies 1953, p. 351).

Sharp & Dohme, Division of Merck & Co., Inc., Philadelphia.

Ophthalmic Ointment Hydrocortone Acetate: 3.5 gm. tubes. An ointment containing 15 mg. of hydrocortisone acetate in each gram.

Ophthalmic Suspension Hydrocortone Acetate: 5 cc. dropper bottles. A suspension containing either 5 or 25 mg. of hydrocortisone acetate in each cubic centimeter. Preserved with 0.5% benzyl alcohol and 0.02% benzalkonium chloride.

Isoniazid (See New and Nonofficial Remedies 1953, p. 85).

American Pharmaceutical Company, New York.

Tablets Isoniazid: 50 mg.

Nepera Chemical Company, Inc., Yonkers, N. Y.

Tablets Pyrizidin: 100 mg.

Mersalyl Sodium and Theophylline (See New and Nonofficial Remedies 1953, p. 307).

C. F. Kirk Company, New York.

Solution Mersalyn with Benzyl Alcohol 2%: 2 cc. ampuls and 10 cc. vials. A solution containing 0.1 gm. of mersalyl (equivalent to 40 mg. of mercury) and 50 mg. of theophylline in each cubic centimeter.

Methamphetamine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1953, p. 196).

Biorganic Laboratories, Inc., East Paterson, N. J.

Powder Methamphetamine Hydrochloride: Bulk; for compounding or manufacturing use.

Phenylephrine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1953, p. 201).

Winthrop-Stearns, Inc., New York.

Ophthalmic Solution Neo-Synephrine Hydrochloride 10%: 4 cc. tubes. A buffered solution containing 0.1 gm. of phenylephrine hydrochloride in each cubic centimeter. Preserved with 0.4% chlorobutanol and 0.3% sodium bisulfite.

Sodium Ascorbate (See New and Nonofficial Remedies 1953, p. 505).

Standard Pharmaceutical Company, Inc., New York.

Solution Sodium Ascorbate: 2 cc. and 5 cc. ampuls. A sterile aqueous solution containing sodium ascorbate equivalent to 50 mg. and 100 mg., respectively, of ascorbic acid in each cubic centimeter. Preserved with 0.4% chlorobutanol and 0.2% sodium bisulfite.

Sulfadiazine-U.S.P. (See New and Nonofficial Remedies 1953, p. 100).

Rexall Drug Company, Los Angeles.

Tablets Sulfadiazine: 0.5 gm.

COUNCIL ON FOODS AND NUTRITION

ACCEPTED FOODS

The following products have been accepted as conforming to the rules of the Council.

JAMES R. WILSON, M.D., *Secretary.*

Buitoni Foods Corporation, New York.

Buitoni Defatted Wheat Germ.

Ingredients: Defatted wheat germ (removed in the processing of flour).

Analysis (submitted by distributor).—Total solids 93.0%, moisture 7.0%, ash 5.5%, fat (ether extract) 0.85%, protein (N × 6.25) 35.8%, crude fiber 2.5%, and carbohydrate (by difference) 48.35%.

Vitamins and Minerals	Mg. per 100 Gm.
Thiamine	3.28
Riboflavin	0.78
Niacin	5.4
Pyridoxine	1.2
Pantothenic Acid	3.38
Biotin	0.03
Inositol	760
Choline	406
p-Aminobenzoic Acid	0.47
Calcium	62
Phosphorus	1,400
Iron	11.6
Potassium	1,100
Magnesium	353
Manganese	9
Copper	1.4

Use.—As a food supplement, providing the nutrients of wheat germ as indicated above, that may be eaten alone as cereal or in combination with other foods.

Prince Macaroni Manufacturing Company, Lowell, Mass.

Egg Pastina

Ingredients: Fancy durum wheat flour, egg solids, thiamine, riboflavin, niacin, and iron phosphate.

Analysis (submitted by manufacturer).—Total solids 90%, moisture 10%, ash 0.79%, fat 3.70%, protein (N × 5.7) 13.03%, crude fiber 0.35%, and carbohydrates other than crude fiber (by difference) 72.1%.

Vitamins and Minerals	Mg. per Hundred Grams
Thiamine	0.9
Riboflavin	0.4
Niacin	5.9
Calcium	35
Phosphorus	194
Iron	3.5

Calories.—3.7 per gram; 105 per ounce.

Use.—In the feeding of infants and older children.

Carrot Pastina

Ingredients: Fancy durum wheat flour, carrots, thiamine, riboflavin, niacin, and iron phosphate.

Analysis (submitted by manufacturer).—Total solids 89.9%, moisture 10.1%, ash 0.87%, fat 1.75%, protein (N × 5.7) 12.26%, crude fiber 0.60%, and carbohydrates other than crude fiber (by difference) 74.42%.

Vitamins and Minerals	Mg. per Hundred Grams
Thiamine	0.9
Riboflavin	0.4
Niacin	5.9
Calcium	38
Phosphorus	160
Iron	3.7

Calories.—3.7 per gram; 105 per ounce.

Use.—In the feeding of infants and older children.

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RESIDUALS OF VIRAL HEPATITIS

While considerable interest has been directed toward the possible after effects of acute hepatitis, conflicting reports have appeared concerning the incidence of long-term residuals in this disease. To throw further light on this subject, Zieve, Hill, Nesbitt, and Zieve evaluated the hepatic function of 367 male veterans from the Minneapolis-St. Paul metropolitan area who had had acute viral hepatitis four to six years previously and compared the results with those obtained on a control group of corresponding size.[1] In the hepatitis group, there were 144 clear-cut cases of serum hepatitis and 186 cases of infectious hepatitis. Twenty-six men had had multiple attacks of hepatitis, either distinctly separate attacks or recurrences. In the remaining persons, the type of hepatitis was unknown. In the group that had not had hepatitis, there were 137 men who during army service had been heavily exposed to viral hepatitis without becoming jaundiced or showing any other signs of infectious hepatitis. There were also 212 persons who had not been exposed in endemic or epidemic areas of hepatitis and who had no history of jaundice, liver disease, syphilis, malaria, yellow fever vaccination, blood or plasma transfusion, or serious injury. In addition, data were available from 69 persons with multiple attacks of hepatitis or prolonged acute episodes. About half of these were not included in the hepatitis sample of 367 cases but were drawn from outside areas because they were known to have had severe attacks. The following determinations were made on all subjects: serum bilirubin; thymol turbidity; cephalin-cholesterol flocculation; colloidal red; total cholesterol, cholesterol esters, and per cent esters; sulfobromophthalein (Bromsulphalein) retention; hippuric acid excretion; galactose retention; urine urobilinogen; and urine coproporphyrin. Needle biopsies were also performed on 60 persons who had had hepatitis and on 16 with no history of hepatitis. In analyzing the data, the following variables were considered: age, weight, body surface area, interval since reference illness, duration of reference illness, urine volume of 24 hour specimen, urine volume of one hour hippuric acid specimen, and alcohol intake before, during, and since service.

The data presented in this study show no appreciable differences in liver function tests between the infectious hepatitis and the serum hepatitis groups other than a significantly greater average zinc sulfate turbidity in the infectious hepatitis cases and significantly higher total cholesterol and cholesterol ester concentrations in the serum hepatitis cases. The latter difference, however, could be accounted for by the significant age difference between the two groups. Comparisons between the maximally exposed and nonexposed control groups reveal minor differences only, such as could be the result of the significantly greater alcoholic consumption by the maximally exposed group. When the data from all hepatitis and all control cases are compared, the only quantitative tests showing significant differences between means are the zinc sulfate turbidity and the total and esterified cholesterol. The larger mean zinc sulfate turbidity values for the hepatitis group are due entirely to the infectious hepatitis cases, while the higher cholesterol values in the hepatitis cases are due largely if not entirely to age differences between the hepatitis and control groups. In addition, there were more non-zero 48 hour colloidal red readings among the hepatitis than among the control cases and more abnormal thymol turbidity values among the infectious hepatitis than among the serum hepatitis or control cases. Results in the multiple or prolonged attack cases were in line with those found in the larger group of all hepatitis cases. The liver biopsies were normal in all but two of the hepatitis and four of the control cases. With the exception of single cases of nonspecific granuloma in each group, the abnormalities could be correlated with excessive alcoholic intake.

In essence, the various groups studied failed to reveal differences by tests measuring hepatocellular dysfunction or by liver biopsies. Thus the occurrence of functional or structural abnormalities among the men who had viral hepatitis four to six years previously was no greater than in the control group. However, the study was limited to male veterans who had icteric viral hepatitis, and the possible outcome of the disease in different age groups and sexes and of nonicteric hepatitis is not necessarily clarified by these studies. The differences that did exist between these two groups lay in tests reflecting changes in serum proteins or lipoproteins, and the authors felt these changes were related to certain immunologic residuals of viral hepatitis. Further, the differences observed in the infectious hepatitis group indicate a difference between the immune responses to the two viruses and are in agreement with earlier reports that the response to the infectious hepatitis virus is more intense and prolonged than that to serum hepatitis virus.[2]

1. Zieve, L.; Hill, E.; Nesbitt, S., and Zieve, B.: Incidence of Residuals of Viral Hepatitis, Gastroenterology **25**: 495, 1953.
2. Green, P.: Some Serochem cal Differences Between Homologous Serum Hepatitis and Infectious Hepatitis, Canad. M. A. J. **63**: 365, 1950. Viral Hepatitis, editorial, J. A. M. A. **152**: 612 (June) 1953.

A CONFUSION OF TONGUES

As if it were not difficult enough for the overburdened medical student to learn what amounts to a complete new language, he is confronted with a gaggle of eponyms, synonyms, and terms, which, although declared officially obsolete 30 years ago, still bob up with amazing persistence. In his basic science courses the student is usually started on the right track. In anatomy he is taught the Basle Nomenclature, in bacteriology the Bergey classification, and in pharmacology the official names of drugs. Often, however, when he reaches the clinical subjects it is as if he had parachuted into a foreign country where his bright new vocabulary is poorly understood and where he must learn the language of his calling anew or fall by the wayside. Because the teachers of the clinical subjects are often regarded by the student with a great deal more reverence than those in the less glamorous basic sciences and because they have the last word, their terminology, confusing as it may be at first, is likely to become indelibly implanted on the students' minds, and thus passive resistance to progress is carried to another generation. When later these students find themselves in practice and write for publication they write as they think and it takes eternal vigilance and a strong crusading spirit on the part of medical editors to catch every reference to a dorsal vertebra (literally a vertebra of the back) and change it to thoracic vertebra, which has a much clearer meaning, and to change every malar bone to zygoma.

Although those who persist in fighting against any innovation are resisting a fundamental law of life and although they cannot prevail forever, they can add greatly to the confusion of the oncoming generation of students. With the publication in 1923 of the first edition of Bergey's "Manual of Determinative Bacteriology" a monumental effort was made to bring order out of chaos in the taxonomy of bacteria. A large portion of this book is now devoted to listing for each organism the many names that have at one time or another been applied to it. Many bacteriologists while accepting and using some of the terminology of the manual in their writing have rejected others. Their reasons may be excellent, but a better impression would be created if they presented a united front and accepted all the preferred names in the manual. Then if they wished to carry on a vigorous campaign among other bacteriologists they might, if their reasons were valid, succeed in having changes adopted in subsequent editions.

When a disease is first described by an author, the author's name frequently becomes attached to the disease. Real confusion has arisen more than once in the past when an especially observing author has described more than one disease and had his name attached to them all. Despite the growing use of the Standard Nomenclature of Diseases and Operations, which has done so much to systematize the naming of diseases, eponyms die hard. One well-loved professor of surgery, of blessed memory, was so fond of eponyms, particularly the double threat or hyphenated type, such as Osgood-Schlatter's disease, that he could not get used to not using them and was heard on several occasions to speak of Lobar-Pneumonia's disease. Such was his personal magnetism that nobody laughed, and it is doubtful that he was ever aware of the slip.

Another cumbersome bugbear of the student, whose capacity for overcoming confusing obstacles is exceeded only by his eagerness to learn, is the time-honored apothecary system of weights and measures. The U. S. Pharmacopeia, the Dispensatory, and most other books on drugs now give preference to the metric system, but pharmacists still are asked to fill prescriptions every day written in the apothecary system, and doses so written still find their way into manuscripts submitted for publication. The confusion over dosage is only one of the student's worries in the field of drugs. New remedies are frequently developed by a pharmaceutical house and marketed under a protected name. This name is widely advertised and may have an unopposed field for several years; however, often other companies here and abroad learning the composition and observing its popularity bring out the same drug under their own protected name. The resulting confusion is by no means limited to medical students but affects nearly everyone connected with clinical medicine.

Because there will always be changes in nomenclature in the various fields of medicine, it behooves all who teach or who write even an occasional article to support by consistent use those terms found acceptable by those who have devoted their talents to choosing the most descriptive terms available.

CONFERENCE ON TRICHINOSIS

The second National Conference on Trichinosis brought together in the auditorium of the American Medical Association in Chicago outstanding authorities on various phases of this subject. The incidence of trichinosis in the United States exceeds that in many other civilized countries, and since the disease is preventable this fact should serve to dissipate smugness regarding high sanitary standards in this country. The incidence of trichinosis in the human population is far greater than is indicated by the number of reported cases. It is conservatively estimated that 25% of all Americans during their lifetime will harbor trichina larvae in their muscles.[1] A representative of the National Live Stock and Meat Board made a plea for steps to prevent through better education unsound, sensational, and misleading articles from appearing in widely circulated popular magazines, the effect of which is to reduce the consumption of pork, a beneficial food necessary to the health and economy of the nation. It was stressed that in an intensification of the education of the public greater use should be made of the cartoon and comic strip approach to reach children, thereby giving them authentic information at a time of life when they are most impressionable. It was also suggested that more use be made of the pulp magazines as a medium for informing a larger segment of the population.

1. Gould, S. E.: Trichinosis: Major Health Problem in United States: What Shall Be Done About It? Bull. New York Acad. Med. **21**: 616-624 (Nov.) 1945.

Since garbage is one of the chief means of transmitting the trichina larvae or "garbage worms" to hogs and rats, the sanitary disposal of garbage was considered at great length. Garbage may be kept away from the animals altogether by various means, the cheapest and most practical way being burial, with use of the method known as the sanitary fill. The chief drawback to this method is in obtaining the consent of the community for a suitable site for this purpose within a reasonable distance from the center of population. Such an operation properly conducted creates no nuisance, but some influential voters do not realize this and are often stubbornly unwilling to be convinced. On the other hand, trichinosis can be controlled if all garbage fed to hogs is boiled for 30 minutes. All but a few states now have laws prohibiting the feeding of raw garbage to hogs, the interstate shipment of raw garbage, or the interstate shipment of hogs fed on such garbage. This legislation, long sought as a means of controlling trichinosis, was passed only when a virus disease affecting hogs but not man and called vesicular exanthem became a serious economic problem for the farmers. Should a vaccine against this disease or any other effective control measure be discovered the laws relating to raw garbage may be repealed.

Another means of attacking trichinosis is treatment of the infected pork. Chilling the carcass at –37 C for two minutes kills the parasites but appears to make the meat slightly less palatable. Prolonged storage in the household deep freeze unit is also effective but likely not to be uniformly reliable. Some countries with a very low incidence of trichinosis rely on microscopic examination of samples of hog diaphragm to reveal the infection in pork. The fact that this method is geared to countries in which raw or undercooked pork is habitually eaten, which is not true of the United States, and that the method would be very expensive if applied here makes it impracticable for use in this country.

A new method, which is not yet developed commercially, will, when put into large-scale operation with designs already perfected, increase the cost of pork by only ⅕ cent a pound. This method consists of subjecting the carcass to gamma irradiation. A dose of 10,000 r has been found to be effective, but in order to provide an ample factor of safety 30,000 r is advised. The advantages of this method are that it (1) is sanitary, (2) is simple and rapid, (3) is completely effective, (4) reduces the spoilage rate of the meat but does not affect its palatability, (5) is safe in that it induces no secondary irradiations, (6) obviates the need for other types of processing, and (7) should increase public acceptance of pork products.[2] Since for economy a plant using this process would have to be large and centrally located, receiving carcasses from many small producers, a system similar to the large milk pasteurizing and bottling plants found in most cities would probably have to be set up. Also, like pasteurization, it would not be a substitute for proper sanitary precautions.

The conference recommended improvement of the reporting of cases of trichinosis; continued admonition to all who cook pork, for the present at least, to follow the time-honored custom of making sure that all pork is cooked until well done before serving; and, because small portions of pork remaining in the butcher's grinder may get into ground beef and veal, a requirement that butchers use a separate grinder for pork. Although it is recognized that there is a wide gap between recommendations and fulfillment, the conference has clearly pointed toward a solution of a vexing problem.

GAMMA GLOBULIN AND POLIOMYELITIS

Reports on the use of gamma globulin as a prophylactic agent for paralytic poliomyelitis have been published previously in THE JOURNAL.[1] All these reports offered promise. None implied that gamma globulin provides the best possible means of preventing paralytic complications following the development of anterior poliomyelitis, but all left the reader with the suggestion that gamma globulin was worthy of trial.

In this issue (page 1086) is a summary of the report of the National Advisory Committee for Evaluation of Gamma Globulin. The study was sponsored by the United States Public Health Service in collaboration with the Association of State and Territorial Health Officers, the American Physical Therapy Association, and the D. T. Watson School of Physiatrics, affiliated with the University of Pittsburgh School of Medicine. Health departments in 41 states and 4 cities actively collaborated in the study. The committee, with the exception of one member, concluded that the administration of gamma globulin to familial associates with poliomyelitis had no significant influence on severity of paralysis developing in subsequent cases, the proportion of nonparalytic poliomyelitis occurring in subsequent cases in which gamma globulin was given before the onset, and the classic pattern of familial aggregation of cases in the country at large. The committee recommended reconsideration of the present distribution and use of gamma globulin. One member of the committee, whose reports had appeared earlier in THE JOURNAL, stated that most of the gamma globulin was given too late to be expected to have much effect and that the data are not from an experiment set up with suitably chosen controls. He asserted that such data fail to demonstrate whether gamma globulin was or was not effective in the two ways in which it was used.

At best, gamma globulin can be regarded as having only limited usefulness as a prophylactic measure for the paralytic forms of poliomyelitis. However, doubts have been raised concerning any usefulness, and this difference of opinion warrants very careful study of the problem. The medical profession and the public both have a personal interest in the outcome of such a study.

2. Gould, S. E.; Gomberg, H. J., and Bethell, F. H.: Prevention of Trichinosis by Gamma Irradiation of Pork as Public Health Measure, Am. J. Pub. Health **43**: 1550-1557 (Dec.) 1953.

1. Hammon, W. McD.; Coriell, L. L., and Stokes, J., Jr.: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 1. Plan of Controlled Field Tests and Results of 1951 Pilot Study in Utah, J. A. M. A. **150**: 739 (Oct. 25) 1952; 2. Conduct and Early Follow-Up of 1952 Texas and Iowa-Nebraska Studies, ibid. Hammon, W. McD., and others: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 3. Preliminary Report of Results Based on Clinical Diagnoses, ibid. Hammon, W. McD.; Coriell, L. L.; Wehrle, P. F., and Stokes, J., Jr.: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis: 4. Final Report of Results Based on Clinical Diagnoses, ibid. **151**: 1272 (April 11) 1953.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

During my travels I frequently hear rumors that are unfavorable to medicine. Unfortunately, these are accepted as gospel truth by many who should know better, including physicians. It reminds me of the man who made his fortune in wildcat oil wells and finally went to his reward. At the Pearly Gates he was informed by St. Peter that admittance to heaven was based on a quota system and he was asked to identify himself by occupation.

"I am a wildcat oilman," he told St. Peter. The custodian of the Pearly Gates checked his records carefully and informed the applicant that he could not be admitted because "the quota for wildcat oilmen is filled." Whereupon the wildcatter made an intensive plea for "just a few moments" inside the gate.

"I'm sure that I can find some little corner for myself in the wildcatters' section," he said. "If not, I'll come right out." St. Peter agreed to this. After about 15 minutes there was a great commotion and a large group of men came charging out of the Pearly Gates. At their heels was our friend. He was stopped by St. Peter, who inquired where the others were going.

"Oh, I started a rumor that they struck oil in hell," the wildcatter replied. "And where are you going?" St. Peter asked. "Well you never know," came the response, "there might be something to that rumor."

Medical men in particular should not be susceptible to false stories about their own profession. They should gather the facts and then present them accurately. We have a great humanitarian story to tell. We have contributed invaluable knowledge and service to the public, and our job is to disseminate this information in its proper light. But when self-appointed spokesmen step into the picture, confusion is the main result. Because some of these persons base their public utterances on poorly documented information, they cause much harm to the medical profession.

Recently there have been too many spokesmen without portfolio expressing strong opinions on controversial issues. Many of these persons have a self-inflated sense of responsibility and a fine disregard for the impact of their remarks—well-intentioned as they might be. The critics of organized medicine within our own profession are often as vociferous and just as badly informed as some of our lay critics. Impatience, ignorance, and anxiety frequently send them racing to the public press and the air waves with broiling pronouncements that cause adverse reactions that require many months to overcome.

I have become impatient with some doctors who are too busy to attend county medical meetings and to devote any of their time to civic activities, but who can always find the time after the golf game is ended to compose a scorching letter to the President of the American Medical Association, or to other officials, on a subject of which they have little knowledge.

All but 9,000 of this nation's physicians in active, private practice are members of the A. M. A. It is an organization that provides equal representation to all members through its House of Delegates, which is organized and operated in much the same fashion as the Congress of the United States. You are the A. M. A. You elect the delegates to the state associations and to the A. M. A. For that reason I believe that the policies of American medicine can be determined best by the House of Delegates of our Association. Your voice should be heard through the members of the House. If they do not represent your views perhaps it is because they do not know them—you did not bother to express them. The general officers of the A. M. A. are elected by the House of Delegates. If they are not satisfactory they can be turned out of office, but they cannot make policy for the Association. Only the House can do this.

I hope that every physician will assume as his or her personal responsibility the task of becoming thoroughly acquainted with our positive program. In addition, each doctor should keep well informed on the socioeconomic aspects of medicine. Equipped with this armamentarium, individual practitioners could give effective help in plugging information gaps that might otherwise be unheeded.

We must at all times be adequately prepared to pass along correct information about what is going on in medical practice My appeal to you is that we work together and make effective use of the one medium that we can share in bringing to the public and the press and periodicals the real story of our efforts to be good citizens and good doctors. That medium is the American Medical Association.

EDWARD J. MCCORMICK, M.D., Toledo, Ohio.

ORGANIZATION SECTION

STATEMENT OF DR. LOUIS H. BAUER ON H. R. 7914 AND S. 1748 BEFORE SUBCOMMITTEE OF HOUSE OF REPRESENTATIVES

I am Dr. Louis H. Bauer of Rockville Center, New York. I am President of the American Medical Education Foundation, and a member of the Board of Trustees of the National Fund for Medical Education. I am also the immediate past-president of the American Medical Association and am appearing here today as a representative of that Association concerning H. R. 7914, 83d Congress, and S. 1748, 83d Congress.

The American Medical Association endorses H. R. 7914, 83d Congress. However, before discussing the provisions of the bill, I should like to review briefly the history of the interest of the American Medical Association in the field of medical education.

The fine quality of medical education in the United States today has resulted directly from the medical profession's efforts over the past 50 years to protect the public against unqualified, poorly trained doctors and from its positive efforts to insure sound training and academic freedom.

To assure an adequate supply of physicians in this country the American Medical Association has actively encouraged expansion of existing medical schools and the construction of new facilities in certain areas. We realize that the resulting increase in enrollments, the expansion of teaching programs, and the rising costs of operations have created major financial problems in some instances.

In order to help meet these financial problems, in the spring of 1949 a group of medical educators, businessmen, representatives from the American Medical Association, and the Association of American Medical Colleges, established a fund known as the National Fund for Medical Education. This organization was established to serve the broad purpose of raising funds from voluntary private sources and distributing them to medical schools. It is for this organization that H. R. 7914 would provide a federal charter of incorporation.

In addition, in December, 1950, the American Medical Association established the American Medical Education Foundation to raise funds from individual physicians and medical groups. These two organizations are separate and distinct, although they cooperate very closely to meet the over-all problem of raising funds for medical education. The National Fund for Medical Education serves as the distributing agency for the money raised by both agencies.

It is the belief of the founders of these two organizations that sufficient funds can be raised from private sources, on a voluntary nationwide basis, to solve the financial problems of the medical schools. The two organizations have cooperated very closely in working toward this objective and have received the strong support and cooperation of the medical profession and industry.

The profession's acceptance and support of this program has increased each year. At the end of 1953 the American Medical Education Foundation recorded a gross return of $1,089,962. In 1951 the foundation received 1,853 contributions; in 1952 it received 7,259, a 287% increase; and in 1953, it received 18,176, an increase of 149% over the previous year. I would like to emphasize that inasmuch as the American Medical Association pays all of the administrative costs of the fund, all contributions received by this foundation go for medical education. In addition, the American Medical Association as an organization has donated $2,000,000 in four successive grants to this project.

The committee may also be interested to know that, in addition to these amounts, during the past year approximately 30,000 doctors made contributions direct to the nation's medical schools, for unrestricted use.

The National Fund for Medical Education, to which H. R. 7914 would grant a federal charter, has, as of July, 1953, contributed $4,764,152 to the nation's medical schools. It is encouraging to observe the increasingly greater support which the National Fund for Medical Education is receiving from industry and other nonmedical sources throughout the country. This increased success also serves to bear out the statement by President Eisenhower that "The National Fund for Medical Education is the practical vehicle for securing the support of American industry for all 79 medical schools."

Medical schools report that grants received from the fund and individual physicians have enabled them to secure additional teachers and retain others, purchase equipment, and expand teaching facilities.

We are convinced that the granting of a federal charter would lend prestige to the National Fund for Medical Education and aid it in its purpose of financing medical education needs from private, rather than governmental sources.

The two bills before the subcommittee today differ in certain respects. As I have indicated, the American Medical Association approves H. R. 7914; it objects to certain of the provisions of S. 1748. Specifically, H. R. 7914 provides that the purposes of the corporation shall be "to raise from private sources, disperse and administer funds for medical education and in connection therewith" to promote and foster certain named objectives, while S. 1748 does not include, as a stated purpose of the corporation, the raising and disbursing of funds from private sources. In addition, H. R. 7914 would provide for the inclusion of four physicians on the Board of Trustees of the corporation.

HOUSE OF DELEGATES

This is one of a series of brief statements explaining the work of various departments of the American Medical Association. —ED.

The House of Delegates is the policy-making body of the American Medical Association. It is a truly democratic body, made up of elected representatives of the various state and territorial medical associations and sections of the Scientific Assembly and representatives of the government medical services. The provisions of the constitution and bylaws permit each constituent state and territorial association to have one representative in the House of Delegates for each 1,000 members or fraction thereof from the respective state or territory. Each section of the Scientific Assembly is allowed one delegate. Ex officio members without the right to vote are the general officers, the past presidents, the past trustees, the general manager, the Editor of THE JOURNAL, and the Assistant Secretary of the Association. The apportionment of delegates from the constituent associations is based on the count, made at American Medical Association headquarters as of Dec. 31 each year, of active members of the societies so reported by the respective secretaries. Delegates from the state and territorial associations are elected for two year terms effective as of Jan. 1 following their election. To be eligible the delegate must have been a member of the American Medical Association for at least the two years prior to his taking his seat in the House. The House meets twice each year during the annual and clinical meetings of the Scientific Assembly. Special sessions of the House of Delegates may be called by the Speaker on written request of 25 or more delegates representing one-third or more of the constituent associations or on the request of a majority of the Board of Trustees. At present the House consists of 165 delegates from state and territorial associations, 20 from scientific sections, and 5 from the government medical services (Army, Navy, Air Force, Public Health Service, and Veterans Administration).

The House of Delegates is presided over by a Speaker and a Vice-Speaker, who are elected from the delegates for one year terms at each annual session. At each session of the House the Speaker appoints the following reference committees: Credentials, Amendments to the Constitution and By-Laws, Hygiene and Public Health, Legislation and Public Relations, Medical Education and Hospitals, Sections and Section Work, Rules and

Order of Business, Reports of Board of Trustees and Secretary, Industrial Health, Reports of Officers, Executive Session, Miscellaneous Business, Insurance and Medical Service, and Medical Military Affairs. In addition, the speaker may ask permission of the House to appoint such special reference committees as he may think necessary for the proper and orderly transactions of the business of the House.

The reference committees meet at times when the House is not in session, and notice is given in the House of Delegates Handbook as well as on a bulletin board in the House as to the location of meeting rooms. Any member of the American Medical Association may appear before these committees to listen or to give testimony. In fact, the various committees welcome this. The only exception to this is when a committee goes into executive session, which is rare except during the time of the preparation of certain of their reports to the House. The affairs of the Association are handled in the same democratic manner that has been the backbone of our parliamentary procedure in the governing legislative agencies of our country.

ACCREDITATION OF HOSPITALS

The Joint Commission on Accreditation of Hospitals has released its annual list of fully and provisionally accredited hospitals in the United States, its possessions, and in Canada. The commission gave full accreditation to 2,920 hospitals and provisional accreditation to 498, a total of 3,418. The list is the first published by the Joint Commission since it took over the actual hospital survey work from the American College of Surgeons Jan. 1, 1953. The commission is supported by the American College of Physicians, the American College of Surgeons, the American Hospital Association, the American Medical Association, and the Canadian Medical Association. The director is Dr. Edwin L. Crosby, whose office is in Chicago.

The Joint Commission is a voluntary effort by leading health organizations to improve the standards of hospital care through a system of self-evaluation. The accreditation program was started in 1919 by the College of Surgeons and was taken over by the Joint Commission as a cooperative effort in 1953. The 1953 list of accredited hospitals includes, as well as those actually surveyed by the commission staff during the year, other hospitals not surveyed during 1953 but approved by the College of Surgeons as of Dec. 31, 1952. Mental hospitals were surveyed by the Central Inspection Board of the American Psychiatric Association and accredited by the commission in cooperation with the American Psychiatric Association. Before being surveyed for accreditation the hospital itself must request such action. Hospitals with less than 25 beds are not eligible for accreditation. It was not possible to visit all hospitals that requested accreditation during the year. There is no charge to the hospital for the accrediting service, the cost being borne by the participating organizations. The program costs about $500,000 annually.

Before a hospital can be accredited, the commission must determine that, among other things, it has a safe and adequate physical plant, with special concern as to fire hazards; that its governing board is properly organized and assumes final responsibility for all aspects of the hospital operation; that its medical staff is organized properly and through regular medical staff meetings reviews the clinical work in the hospital; that all tissue removed at operation is reviewed regularly to determine the adequacy and justification of the surgical work in the hospital; and that adequate medical records are made promptly and preserved. Full accreditation means that a hospital meets the required standards of the commission. Provisional accreditation means that the hospital fell just short. Such hospitals are resurveyed within one year to determine if they have corrected the deficiencies shown in the original survey.

RESERVATIONS FOR FLIGHT TO SAN FRANCISCO

The Chicago Medical Society announces a special air transportation plan to the American Medical Association Annual Meeting in San Francisco and a trip to Hawaii after the meeting. The outbound flight leaves Chicago at 12:00 noon Sunday, June 20. A flight to Hawaii leaves San Francisco Friday night, June 25. The return to Chicago is scheduled for July 4. A few reservations are available. Those interested may contact Dr. Elmer V. McCarthy, Transportation Chairman, Chicago Medical Society, 86 E. Randolph St., Chicago.

FEDERAL MEDICAL LEGISLATION

Lengthening of Presumption of Service-Connection for Active Tuberculosis, Multiple Sclerosis, and Chronic Functional Psychoses

Senator Martin (R., Pa.), on request, has introduced a bill, S. 3012, which would provide that "active pulmonary tuberculosis or all other types of active tuberculosis, multiple sclerosis, or any of the chronic functional psychoses developing a 10 per centum degree of disability or more within three years from the date of separation from active service, shall, in the absence of affirmative evidence to the contrary," be deemed service connected. The present law provides a limit of service-connection of one year for psychoses, two years for multiple sclerosis, and three years for all types of tuberculosis, except pulmonary. Pulmonary is included under the Martin bill. The bill is identical with H. R. 6931, introduced by Congresswoman Rogers (R., Mass.), and virtually identical with H. R. 33, also introduced by Mrs. Rogers. Both Rogers bills have been previously reported. The present bill was referred to the Senate Finance Committee.

Voluntary Social Security Extension for Professional Persons

Congressman Golden (R., Ky.) in H. R. 8079 would extend social security coverage on a voluntary basis to professional persons, such as physicians, lawyers, dentists, osteopaths, veterinarians, chiropractors, naturopaths, optometrists, Christian Science practitioners, and others. He provides also in the bill for "old-age insurance benefits for certain permanently and totally disabled individuals under the age of sixty-five, to provide that no deductions from benefits shall be made on account of outside earnings." This bill was referred to the Ways and Means Committee.

Hill-Burton Expansion

After hearings on H. R. 7341, and repeated committee executive sessions, the House Interstate and Foreign Commerce Committee, through Chairman Wolverton (R., N. J.), have reported favorably a new bill, H. R. 8149, which supersedes H. R. 7341 previously reported. The new bill provides for expansion of the Hill-Burton hospital construction program to include diagnostic or treatment centers, hospitals for the chronically ill, rehabilitation centers, and nursing homes. The same amount of appropriations are asked: 182 million dollars over a period of three years; of this amount, 2 million would be for planning and surveys, 20 million annually for diagnostic or treatment centers, 20 million annually for hospitals for the chronically ill, 10 million annually for rehabilitation facilities, and a like amount for nursing homes. Administration will be by states, under regulations drawn up by the Surgeon General of the U. S. Public Health Service. The regular Hill-Burton procedure for matching will be followed, except that a state may decide on a 50-50 matching program. Added to the new bill, is a restatement of the purpose of the original Hill-Burton law to help states to provide facilities "for furnishing to all their people adequate services." This apparently would rule out facilities sponsored by a labor or fraternal organization or a prepaid health plan unless the general public were allowed full and unrestricted use of the facilities. Centers or hospitals to receive the grants must be public or other nonprofit centers or hospitals. Centers and nursing homes to be eligible must be "under the professional supervision of persons licensed to practice medicine in the state," or they "must be operated in connection with a hospital." Diagnostic treatment centers, unless public, will have to be operated by or be a part of "a corporation or association which owns and operates a nonprofit hospital." In the facilities used by more than one state, a state may transfer part of its allo-

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The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

cation to the state in which the facility is to be constructed. If a facility were sold or transferred, at any time, the U. S. government would have authorization to recover its proportionate share of a facility converted to private use. This bill was referred to the Interstate and Foreign Commerce Committee, passed by the committee, and referred back to the floor of the House with a recommendation that it be considered favorably.

National Mental Health Week

Senator Smathers (D., Fla.) and 51 other senators in S. J. Res. 130 request the President to proclaim May 2 to May 8, 1954, as National Mental Health Week and to urge the public to cooperate in the fight for prevention and cure of mental illness. Identical bills were introduced in the House by Brownson (R., Ind.) in H. J. Res. 384 and Garmatz (D., Md.) in H. J. Res. 449. These bills were referred to their responsible judiciary committees.

Alaskan Mental Health Act

Senator Butler (R., Neb.) in S. 3037 proposes to modernize the program in Alaska for the commitment and care of the mentally ill. The federal government would continue to bear essential financial responsibilities until Alaska itself could assume the total cost of the care of mentally ill persons in the territory. This bill was referred to the Interior and Insular Affairs Committee.

Expense Deductions by Physically or Mentally Disabled

Congressman Kersten (R., Wis.) would authorize deduction from taxable income of any extraordinary expense "because of any physical or mental disabilities of the taxpayer, taxpayer's spouse, or any dependent of the taxpayer. Such extraordinary expenses shall mean expenses which would not have been incurred by the taxpayer if the disability or disabilities did not exist." The bill was referred to the Ways and Means Committee.

Vocational Rehabilitation Grants

Senator Potter (R., Mich.) proposes to amend the rehabilitation act to make available funds for federal grants for allotment among the states by the Secretary of Health, Education, and Welfare in an amount equal to 100% of a state's expenditures for administrative, guidance, and placement services in the base year 1953 and equal to 50% of the expenditures for rehabilitation services in the base year. Beginning in 1957, such amount shall be 66⅔% of such state's base year expenditures. This bill was referred to Labor and Public Welfare Committee.

Agency for Handicapped

Congressman Radwan (R., N. Y.) by H. R. 8042 would establish a federal agency for the handicapped in the Department of Labor and would abolish the present Office of Vocational Rehabilitation now in the Department of Health, Education, and Welfare. It would provide a 10 million dollar revolving loan fund the first year and 5 million dollars annually thereafter for each of five years, from which states could borrow money at such times as their own funds for vocational rehabilitation were exhausted. This bill, which is identical with 14 other House bills previously reported, was referred to the Committee on Education and Labor.

Rabies

Congressman Sheehan (R., Ill.) by H. R. 8015 would authorize the Surgeon General "to conduct research, investigations, experiments, and demonstrations relating to the diagnosis, cure, prevention, and treatment of rabies and related diseases in animals and in human beings; to assist and foster similar activities by other agencies, Federal, State, or local, public, or private; to cooperate with such agencies in such activities; and to promote the coordination of all such activities and the useful application of their results, with a view to the eventual eradication of rabies and related diseases from the United States." This bill was referred to the Committee on Interstate and Foreign Commerce.

Grants-in-Aid to Philippines for Treatment of Veterans

Congresswoman Rogers (R., Mass.), by request, has introduced a bill that would extend for three additional years reimbursement to the republic of the Philippines for hospitalization of Philippine veterans authorized by Public Law 865, approved July 1, 1948. The bill was referred to the Veterans' Affairs Committee.

STATE MEDICAL LEGISLATION

Arizona

Bills Introduced.—H. 336, proposes to amend the law relating to **narcotic drugs** by making it unlawful for a person to administer to himself a narcotic drug by intravenous injection or other means. S. 130, proposes that in any criminal trial or sanity hearing when it is necessary to have the services of **a psychiatrist to give expert testimony**, the party requesting such testimony shall make his request to the presiding judge and the judge, on determining that the request is reasonable, shall order the hiring of a qualified psychiatrist at a daily rate of not more than $50.

California

Bill Introduced.—S. 40-X, proposes to amend the health and safety code **relating to narcotics** by, among other things, providing that no person convicted of a second, third, or subsequent offense against the narcotic act shall be granted probation by the trial court, nor shall the execution of sentence imposed on such person be suspended by the court. Furthermore, such person shall not be eligible for parole until he has served at least two-thirds of the minimum sentence for the offense for which he was convicted.

Kentucky

Bills Introduced.—H. 290, proposes to **define an orthoptic technician** as a person who trains and directs other persons to engage in ocular exercises designed to correct visual defects. Such a person would not be required to be licensed as an optometrist if such training and direction are done pursuant to and under the instructions of a duly licensed physician, osteopath or optometrist and consist solely of visual training, orthoptics or ocular exercises. S. R. 47, proposes the creation of a committee to study the possibility and desirability of **establishing a medical school** in Northern Kentucky.

Michigan

Bill Introduced.—S. 1255, proposes amendments to the law **regulating the use of narcotic drugs** by among other things requiring every physician who shall examine any person and find that such person is addicted to the use of narcotic drugs to make a **report thereof** to the health officer of the county, city, township, or district in which such person is a resident.

Mississippi

Bills Introduced.—H. 792, to amend the law relating to pharmacies, proposes that no person other than a registered pharmacist or assistant pharmacist shall sell, dispense or furnish any drug the label of which by law or regulation of the state board of pharmacy or federal food or drug administration is required to bear a statement that it is to be dispensed only by or on the prescription of a physician, dentist, veterinarian, or other person licensed to prescribe drugs. S. 1520, proposes the **creation of a cancer committee** of the state hospital commission, whose duty it shall be to decide in which cases operating room fees and blood transfusions shall be paid.

New York

Bills Introduced.—A. 2675, proposes the enactment of a comprehensive statewide system of **health insurance.** A. 3225 and S. 2769 to amend the mental hygiene law relating to membership on mental health boards propose that at least **two of the appointive members of such boards shall be physicians** actively engaged in private practice. S. 2709, proposes that every hospital, infirmary, dispensary, clinic, home or institution for convalescent, invalid, aged, or indigent persons, or a lying-in asylum shall be **liable for damages for personal injuries** sustained by any person or for death resulting **from the negligence or malpractice of a physician,** surgeon, nurse, or other person employed by such institutions. S. 2750, proposes to authorize hospital managers to provide **ambulance service** for bringing patients to or removing them from the hospital. S. 2751, proposes to authorize the governing board of a municipal corporation operating a hospital to provide **ambulance service** in the territory at public expense.

Bill Enacted.—S. 1002, has become Chapter 97 of the Laws of 1954. It amends the education law relating to conditional admission to the medical licensing examination by **adding** as one of the **subjects of the examination bacteriology.**

Rhode Island

Bills Introduced.—H. 770, proposes to authorize the governor to appoint a committee to make a study of the feasibility of **establishing** a permanent **school for attendant or practical nursing.** H. 782, to amend the **basic science act,** would permit applicants to have had at least one year as a commissioned or petty officer in the medical corps of the U. S. armed forces in lieu of one year preprofessional collegiate training. H. 791, to amend the workmen's compensation act, proposes that **no fee shall be paid for major surgery unless** the surgeon has first notified the director of labor, the employer, and the insurance carrier and obtained permission in writing for the operation, except in an emergency. H. 794, declares it to be an obligation of the state to provide for all state employees state paid **hospital and medical services.** H. 820, proposes an **annual registration law** for physicians and osteopaths.

MEDICAL NEWS

ILLINOIS

Public Health Meeting.—At the Illinois Public Health Association's annual conference, April 1-2, Dr. Roland R. Cross, director, Illinois Department of Public Health, Springfield, will deliver the address of welcome Thursday, 9 a. m., at the St. Nicholas Hotel, Springfield, after which Dr. Edward G. McGavran, dean, School of Public Health, University of North Carolina, Chapel Hill, will present "What Is Public Health in 1954?" The afternoon session will comprise a discussion of patterns in citizen participation, in which Drs. Jackson P. Birge, Rock Island, Elvin L. Sederlin, Villa Park, Roger F. Sondag, Murphysboro, and Louis L. Vitt, Canton, will serve as collaborators. After the 6:30 banquet, "Call Me Doctor" will be presented by the division of sanitary engineering, Illinois Department of Public Health. Friday morning Dr. Ruth M. Moldenhauer, division of local health administration, Illinois Department of Public Health, will open the sessions on teamwork in public health with "Cooperation Between Official and Voluntary Health Agencies." Dr. McGavran will deliver the luncheon address "Education of the Professional Public Health Worker" on Friday.

Chicago

Meeting on Thromboembolic Disease.—A joint meeting of the North Side branch of the Chicago Medical Society and the Chicago Heart Association will be held April 1, 8 p. m., at the Drake Hotel. "The Treatment of Thromboembolic Disease" will be presented by Dr. Ovid O. Meyer, professor of medicine, University of Wisconsin Medical School, Madison. Discussion will be by Dr. Wright R. Adams, professor of medicine, University of Chicago School of Medicine, and Dr. Geza De Takats, clinical professor of surgery, University of Illinois College of Medicine. For reservations, call CEntral 6-7764.

LOUISIANA

Symposium on Industrial Medicine.—A symposium on industrial medicine will be presented April 1-2 by the Tulane University of Louisiana School of Medicine, New Orleans, under the cosponsorship of the A. M. A. Council on Industrial Health, American Academy of General Practice, and the Liberty Mutual Insurance companies. On Thursday a general session for physicians and personnel, health education, safety, and administrative officers of industry will cover workmen's compensation, rehabilitation, industrial safety and hygiene, health promotion, absenteeism, nonoccupational disabilities, labor's viewpoint of industrial medical care, and other allied subjects. Presentations by physicians in this program include:

Rehabilitation in, and Outside of, Industry, Jack K. Wickstrom, New Orleans.
Teamwork in Health and Safety, Charles F. Shook, Toledo, Ohio.
Health Promotion and Work Effectiveness, Henry E. Meleney, New Orleans.
Significance of Nonoccupational Disability in Industry, Waldo L. Treuting, New Orleans.

The Friday program will include discussions on such subjects as occupational disease diagnosis, common industrial diseases, fatigue, noise in industry, fundamentals of industrial medical practice, part-time employee health service, surgery in industrial medicine. All sessions will be held in the auditorium of Hutchinson Memorial Medical Building.

MASSACHUSETTS

Tufts Medical Alumni Meeting.—At the annual dinner meeting of the Tufts Medical Alumni Association March 31, 6:30 p. m., at the Hotel Somerset, Boston, the guest speaker will be Arthur S. Flemming, LL.D., Delaware, Ohio, director, Office of Defense Mobilization. Other speakers include Nils Y. Wessell, Ph.D., president of Tufts College, and Dr. Joseph M. Hayman Jr., dean of Tufts College Medical School, Boston. The graduating class of the medical school and the 50 year class (1904) will be guests of the alumni association. The 25 year class (1929) will hold its 25th reunion, March 30-31, in connection with the annual medical alumni dinner meeting. Dr. Edward O. Broderick, Needham, will give an account of this class. Preceding the dinner, there will be open house at the medical school from 10:30 a. m. to 4 p. m.

Seminar on Peripheral Vascular Disease.—This seminar will be presented at Boston City Hospital, March 31. Dr. Eugene E. O'Neil professor of clinical surgery, Boston University School of Medicine, will be chairman for the following program:

Treatment of the Postphlebitic Syndrome, John J. Byrne, Boston.
Buerger's Disease, Edward A. Edwards, Boston.
Treatment of Arterial Emboli, George F. Miller, Boston.
Raynaud's Disease, Charles W. Robertson, Boston.
Treatment of Acute Vascular Injuries, Edward J. Jahnke, Washington, D. C.
Lumbar Sympathectomy in Obliterative Arterial Disease, Reginald H. Smithwick, Boston.
Intimectomy and Autogenous Vein Grafts for Segmental Arterial Occlusions, Gerald H. Pratt, New York.
Arterial Grafting in Peripheral Arterial Disease, Charles A. Hufnagel, Washington, D. C.
Blood Vessel Grafts in the Surgical Treatment of Diseases of the Major Arteries, Robert R. Linton, Brookline.
Use of Fresh and Preserved Grafts for Aneurysms or Obstructive Arterial Lesions, Ralph A. Deterling Jr., New York.

MINNESOTA

Lecture by Dr. Allen.—The Clarence M. Jackson lecture, "The Management of Massive Upper Gastrointestinal Bleeding," will be given by Dr. J. Garrott Allen, professor of surgery, University of Chicago School of Medicine, April 1, on the University of Minnesota campus, Minneapolis. Dr. Allen will also participate in a continuation course in emergency surgery for general physicians at the Center for Continuation Study April 1-3.

NEBRASKA

Postgraduate Assembly.—The second annual postgraduate assembly and Poynter Foundation lecture will be held at the Nebraska University College of Medicine, Omaha, March 29-31. Presentations by out-of-state speakers include:

Diagnosis and Management of Rheumatic Fever in the Childhood Period. Advances in the Field of Infant Nutrition, Arild E. Hansen, Galveston, Texas.
Psychological and Social Problems of Convulsive Disorders in Infants and Children. General Practitioner's Role in Handling the Handicapped Child, Reynold A. Jensen, Minneapolis.
Management of Acute Injuries in the Chest, John H. Mayer Jr., Kansas City, Mo.
Excisional Therapy for Management of Pulmonary Tuberculosis, F. John Lewis, Minneapolis.
Rational Antibiotic Therapy, Harry F. Dowling, Chicago.
Iron Metabolism During Pregnancy, Roy G. Holly, Minneapolis.
Role of Edema in Functional Pelvic Pain, Gerald L. Miller, Kansas City, Mo.
Selective Treatment of Diabetes Mellitus According to Severity, Arthur R. Colwell, Chicago.

The Tuesday program will conclude with a round table on recent advances in infectious diseases, and the Wednesday program with a round table on problems in the management of the geriatric patient. Reuben G. Gustavson, Ph.D., former chancellor of the University of Nebraska, Lincoln, will deliver the Poynter lecture at the alumni dinner at the Fontenelle Hotel.

NEW YORK

Symposium on Trauma.—The Scientific Assembly of the Queens County chapter of the American Academy of General Practice, March 30, in the Medical Society Building, will be devoted to a symposium on trauma. Dr. William E. F. Werner, Rockaway Park, president-elect, will be moderator for the following morning session:

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

Fundamental Physiology and Pathology of Shock, Magnus I. Gregersen, Ph.D., New York.
Present-Day Concepts of Burn Therapy, Edward L. Howes, New York.
Radiation Injury and Its Management, Joe W. Howland, Rochester, N. Y.

A panel discussion will precede luncheon, at which Dr. Michael M. Schultz, Hollis, will serve as chairman, and Dr. Louis Bush, Baldwin, will deliver an address. Panel discussion will also follow the afternoon session, at which Dr. Ferdinand H. Herrman, Far Rockaway, will act as moderator for the following program:

Injuries to Thorax, Duane M. Carr, Memphis, Tenn.
Initial Treatment of Bone and Joint Injuries, John R. Cobb, New York.
Acute Abdominal Injuries, J. Englebert Dunphy, Boston.
Head Injuries, A. Earl Walker, Baltimore.

OHIO

Billroth Surgical Association.—The Billroth Surgical Association will hold a postgraduate assembly March 31 at the Cleveland Health Museum, 8911 Euclid Ave. Reservations should be made before March 29 through Dr. John J. Evans, Secretary, 5504 Superior Ave., HEnderson 1-4731, or Dr. E. Peter Coppedge, Treasurer, 10300 Carnegie Ave., GArfield 1-3740. At 2 p. m. Dr. Aaron E. Kanter, clinical professor of obstetrics and gynecology, University of Illinois College of Medicine, Chicago, will discuss "Hysterectomy—Total, Subtotal, and Vaginal." At 3:30 Dr. Benjamin S. Kline, director of pathology, Woman's Hospital, Cleveland, will present "Demonstration of Gross Pathology of Ovarian and Uterine Tumors." After a 6:30 banquet in the Tudor Arms Hotel ($5 a plate) Dr. Kanter will speak on female endocrinology.

Second Nutrition Conference.—The second Conference on Human Nutrition will be held March 31-April 1 at the Ohio Union, state university campus, Columbus, under sponsorship of the Ohio Nutrition Committee, the Ohio Department of Health, the Institute of Nutrition and Food Technology of Ohio State University, and the Society of Sigma Xi. The program will open Wednesday afternoon with papers on soil, climate, and nutritional value of food; the effect of current processing methods on the nutritive value of foods; and motivation factors in changing food habits. After dinner, 6 p. m. at the union, Dr. Norman H. Jolliffe, New York, will present "Recent Developments in Human Nutrition." Thursday morning Dr. Thomas E. Shaffer, Columbus, will discuss "Nutrition and Growth in Young Children," and Dr. Robert M. Zollinger and staff, department of surgery, will present a symposium on nutrition in surgery. Thursday afternoon Dr. John D. Porterfield III, director of the Ohio Department of Health, Columbus, will discuss "Iodine Deficiency, A Public Health Problem," and Hamilton B. G. Robinson, D.D.S., M.S., associate dean, College of Dentistry, Ohio State University, will consider "The Fluoridization Problem in Ohio."

WISCONSIN

Loevenhart Memorial Lectureship.—The Alpha Psi chapter of Phi Delta Epsilon fraternity at the University of Wisconsin Medical School, Madison, announces that the Arthur S. Loevenhart memorial lectureship on carcinogenesis will be presented at 8 p. m., April 2 in the auditorium of the Service Memorial Institute by Dr. William Boyd, professor of pathology, University of British Columbia, Vancouver, British Columbia, Canada, and author of the textbook on pathology currently used by the medical students.

Gastroenterology Meeting.—The central region of the American College of Gastroenterology will meet in Milwaukee March 28 at the Hotel Schroeder. Dr. Sigurd W. Johnsen, Passaic, N. J., president, American College of Gastroenterology, will preside at the first afternoon session on Sunday, and Dr. Lynn A. Ferguson, Grand Rapids, Mich., president-elect of the national association, at the second session. Presentations by invitation include:

Management of Benign Ulcerative Intestinal Disease, J. Arnold Bargen, Rochester, Minn.
Diagnosis and Treatment of Pancreatic Disease, Philip Thorek, Chicago.
Neurovascular Mechanism of Gastric Ulcer Formation, Hyman B. Benjamin and Marvin Wagner, Milwaukee.

Members of the medical profession are invited.

GENERAL

Foundation Appoints President.—Mr. George Bugbee, executive director of the American Hospital Association, Chicago, has been appointed president of Health Information Foundation (420 Lexington Ave., New York 17) to succeed the late Adm. William H. P. Blandy, who held the position from 1950 until his death Jan. 12. Organized four years ago as a nonprofit organization, the foundation has been supported as a public service by 165 drug, pharmaceutical, chemical, and allied companies. Currently it is engaged in five fact-finding and public relations projects dealing with the costs of medical care and health insurance. Before his service with the American Hospital Association, Mr. Bugbee was director of City Hospital, Cleveland.

Association of American Physicians and Surgeons.—The annual meeting of the Association of American Physicians and Surgeons will be held at Jackson, Miss., April 1-3. Participants in the program will include the Hon. Hugh White, governor of Mississippi; the Hon. J. Bracken Lee, governor of Utah; Dr. Lewis A. Alesen, Los Angeles, past president, California Medical Association; Dr. Francis J. L. Blasingame, Wharton, president-elect, Texas Medical Association; Dr. Monterville Q. Ewing, Amory, president, Mississippi State Medical Association; Dr. Stirling S. McNair, Jackson, president, Central Medical Society of Mississippi; and George S. Benson, LL.D., Searcy, Ark., president, Harding College.

Society for Plastic Surgery.—The American Otorhinologic Society for Plastic Surgery, Inc., will meet March 27 at the Hotel Statler in Boston. At 2 p. m. "The Management of Cleft Palate Cases Involving the Hard Palate, So As Not to Interfere with the Growth of the Maxilla" will be presented by Dr. Fred Squier Dunn, New York (by invitation), with discussion by Dr. Raymond S. Rosedale, Canton, Ohio. Dr. Henry Beinfield, Brooklyn, will have as his subject "Surgical Management of Complete and Incomplete Bony Atresia of the Posterior Nares" (discussion by Dr. Matthew S. Ersner, Philadelphia). Cocktails and dinner are scheduled for 6:30 p. m. "The Management of Congenital Cleft Lip and Associated Nasal Deformities" by Dr. Douglas Parker, New York (by invitation) at 8 p. m. will be followed by round-table discussions on otorhinological problems, with Dr. Nathan A. Bolotow, Providence, R. I., as moderator.

Psychosomatic Society Meeting.—The American Psychosomatic Society will hold its annual meeting March 27-28 at the Jung Hotel, New Orleans. The president, Dr. George L. Engel, Rochester, N. Y., will serve as moderator for a round-table discussion on neoplastic disease and psychological processes, Saturday afternoon. Sunday afternoon Dr. Lawrence S. Kubie, New York, president-elect of the association, will be chairman for a panel discussion "Recent Concepts of Central Neurophysiology: Their Bearing on Psychosomatic Phenomena." Tours through the department of psychiatry and neurology, Tulane University of Louisiana School of Medicine, with exhibits of research in progress, will be conducted on Friday and Monday, and a tour of the research facilities of Southeast Louisiana Hospital at Mandeville, La., will leave Monday at 1 p. m. Films dealing with research work underway at Tulane will be shown Friday, 4-6 p. m., and Monday, 9-11 a. m.

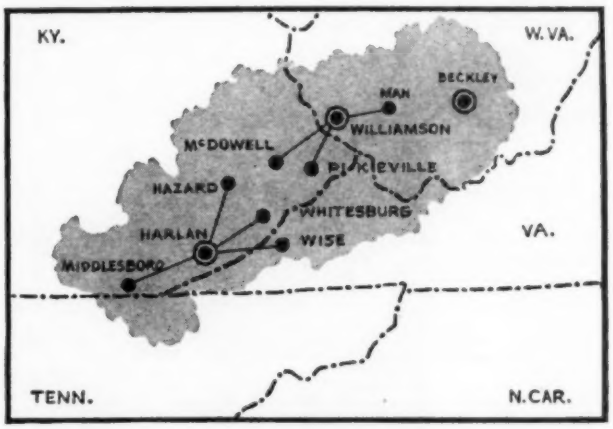
Cancer Conferences.—The annual Mid-West Cancer Conference will be held at the Broadview Hotel, Wichita, Kan., April 1-2 under the sponsorship of the American Cancer Society, Kansas division, and the Committee on Control of Cancer, Kansas Medical Society. Guest speakers include Drs. Axel N. Arneson, St. Louis; Louis H. Clerf, Philadelphia; Warren H. Cole, Chicago; Hugh F. Hare, Los Angeles; Richard H. Overholt, Brookline, Mass.; Norman L. Higinbotham, Cornelius P. Rhoads, and Arthur P. Stout, New York. The day after this conference, the South Central region, College of American Pathologists, and the Kansas Society of Pathologists will sponsor a one day seminar on tumors of the lung, pleura, chest wall, and mediastinum at the same hotel. Dr. Arthur P. Stout, New York, will serve as moderator. Those interested in reviewing the seminar slides before the meeting may obtain them without charge from Dr. Ann Pollak, Kansas University Medical Center, Kansas City, Kan.

Tri-State Medical Meeting.—The 81st annual meeting of the Tri-State Medical Association at the Toledo and Lucas County Academy of Medicine, 3101 Collingwood Ave., Toledo, Ohio, April 1, will be preceded by a telecolor clinic at the academy from 5 to 6 p. m., March 31. The program will concern "Advances in Control of Cancer of the Colon and Rectum." On Thursday a coffee and doughnut hour for physicians and their wives, arranged by the woman's auxiliary of the academy, will be followed at 9:30 a. m. by addresses of welcome by Drs. Bernhard Steinberg, president of the association, and Frank F. A. Rawling, president of the academy, both of Toledo. The program will consist of panel discussions on allergic diseases; office practice in internal medicine; clinical pathological conference; endocrinology; gastrointestinal diseases; and urological diseases. At the luncheon, "The Anatomy of Humor" will be considered by Mr. Allen Saunders, creator of the cartoons "Mary Worth" and "Steve Roper."

Silver Anniversary of Aero Medical Association.—The 25th annual meeting of the Aero Medical Association will be held at the Statler Hotel, Washington, D. C., March 29-31 under the presidency of Rear Adm. Bertram Groesbeck Jr., M.C., U. S. N., retired. Among the participants will be medical officers of Australia, Denmark, Japan, Sweden, England, Italy, Switzerland, and Thailand, whose presentations will include progress in aviation medicine, jet passenger aircraft, and understanding of the "fear of flying syndrome." The traditional Civil Aeronautics Administration forum for airline medical examiners will be held Monday afternoon with Dr. Gerald S. Backenstoe, Emmaus, Pa., as chairman. Topics to be considered include: "What the General Physician Should Know About Aviation Medicine," "Functional Disturbances of the Ear, Nose, and Throat as They Apply to Airmen," "Aviation and Teeth with Special Reference to Aerodontalgia," "A Restricted Medical Certification for Civilian Pilots," "The Selection of the Civilian Flyer," and "The Aged and Retiring Pilot." Dr. John A. Tamisiea, Omaha, will serve as chairman for a panel on the aging pilot at 3:20 p. m. Helicopter evacuation of battle casualties in Korea will be discussed Wednesday morning, as will the detection of anoxia in fatal accidents. At the honors night dinner, Wednesday, 7 p. m., recipients of the Theodore C. Lyster, Raymond F. Longacre, and Arnold D. Tuttle awards for 1953 will be announced.

American Heart Association.—The Staff Conference of Heart Associations has been scheduled by the American Heart Association at the Hotel Morrison, Chicago, March 28-31; assembly panels and the annual meeting at the Conrad Hilton Hotel, Chicago, April 1-2; and the scientific program of the section on clinical cardiology, April 3-4 at the Conrad Hilton. The staff conference will hear a publicity panel "Telling the Heart Story" Monday, 9:30-11 a. m., with Dr. Theodore R. Van Dellen, Chicago, and Dr. Kenneth G. Kohlstaedt, Indianapolis, among the collaborators. On Wednesday Dr. John G. Bielawski, Detroit, will serve as chairman. Dr. Eugene B. Ferris, professor of medicine, Emory University College of Medicine, Georgia, will discuss "Functions of an Affiliate Research Committee," and Dr. E. Cowles Andrus, Baltimore, president-elect, American Heart Association, will present "Research Philosophy of the American Heart Association." The president's address will be delivered at 1:30 p. m. by Dr. Robert L. King, Seattle. On Thursday, the assembly will hear panel discussions on public education and public relations by Dr. George N. Aagaard, Dallas, Texas; professional education by Dr. J. Murray Kinsman, Louisville, Ky., rehabilitation and cardiac-in-industry by Drs. Lewis H. Bronstein, New York, and Richard J. Clark, Winchester, Mass.; and research by Dr. Ferris and by Dr. Eugene A. Stead Jr., Durham, N. C. Friday a community program demonstration and discussion will be presented by the Council on Rheumatic Fever and Congenital Heart Disease. The scientific program of the section on clinical cardiology will open Saturday with "Metabolism of Myocardium," by Dr. W. F. H. M. Mommaerts, Cleveland. Dr. Howard B. Sprague, Boston, will be moderator for a panel on cardiac arrhythmias preceding luncheon, and Dr. Norman E. Freeman, San Francisco, will present "Advances in the Surgical Treatment of Arterial Disease" at 1:30 p. m. The afternoon session will end with a panel on prevention of complications of myocardiac infarction, with Dr. George C. Griffith, Pasadena, Calif., as moderator. The annual dinner and presentation of awards are scheduled for 7:30 p. m. The Sunday session will open at 9 a. m. Luncheon will be preceded by a panel on pathogenesis of atherosclerosis, Dr. Edgar V. Allen, Rochester, Minn., serving as moderator. At 1:50 p. m. Dr. Irving S. Wright, New York, will present the Lasker award to Dr. Albert Szent-Gyorgyi, Woods Hole, Mass. Dr. Irvine H. Page, Cleveland, will give the Lewis A. Conner lecture "An Introduction to Atherosclerosis," at 2 p. m., and at 4 p. m. Dr. J. Russell Elkinton, Philadelphia, will moderate a panel on "Electrolytes and Heart Failure." Former Vice-President Alben W. Barkley and Mrs. Barkley will speak at a special dinner honoring the presidents of affiliated heart associations on Thursday evening. Guest speaker at the annual banquet will be Frank E. Holman, M.A., Seattle, past president of the American Bar Association.

United Mine Workers to Build Ten Hospitals.—In the bituminous mining communities of the mountains of Kentucky, West Virginia, and Virginia, the United Mine Workers of America Welfare and Retirement Fund has underwritten a large scale development that will provide its members with better hospital and medical care. After extensive study by hospital and health authorities, architects, and other experts, the fund decided to establish a chain of 10 hospitals stretching over 250 miles of Appalachian Mountain territory and providing 1,035 hospital beds. The fund sponsored the formation of the Memorial Hospital Association to construct and operate hospitals at Beckley, Williamson, and Man in West Virginia, at Harlan, Middlesboro, Hazard, McDowell, Pikeville, and Whitesburg in Kentucky, and at Wise in Virginia. The number of beds will vary from 50 in the community hospital at Pikeville to 199 at the central hospital at Beckley. Prior to the planning, an advisory committee of outstanding medical authorities visited the mining areas and found that the need for hospital facilities was keenly felt throughout the bituminous coal mining region but it was especially acute where these 10 hospitals are to be built.



The architects were instructed to plan these structures in the most modern design, but at the least expense, that would provide the best of hospital and medical service. It is noteworthy that the design for the Whitesburg Memorial Hospital, prepared by Sherlock, Smith, and Adams of Montgomery, Ala., won the design award in the health category of an architectural design competition conducted by *Progressive Architecture*, a national architectural magazine.

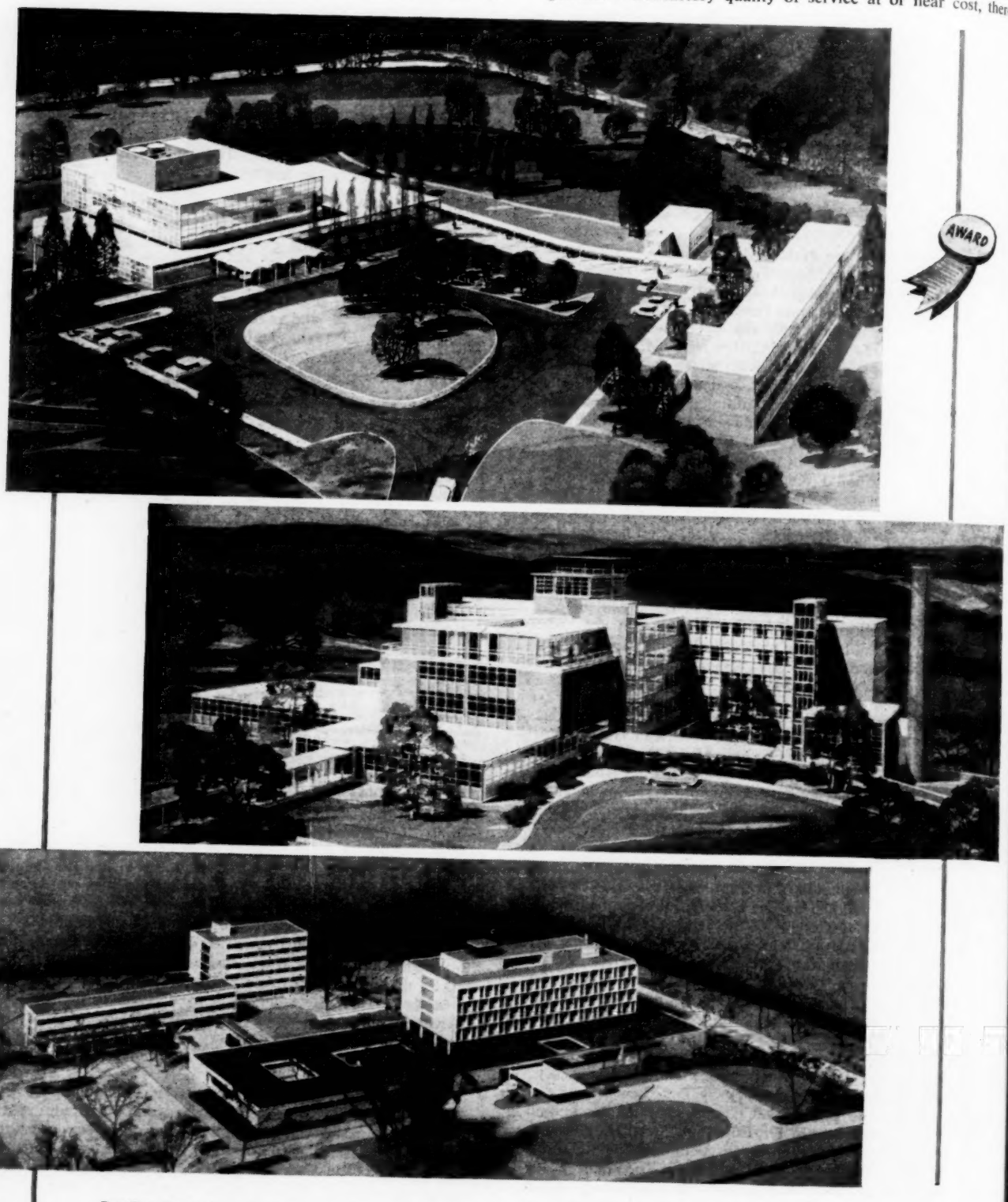
The Memorial Hospital Association is introducing central planning, purchasing, processing, storage, and in certain departments, operation. One innovation will be a central service center that will serve all of the 10 hospitals. The service center, located at Williamson, W. Va., will be 173 miles from the farthest hospital in the chain. The laundry, pharmacy, and some sterilizing will be in one integrated processing and issue system. The central pharmacy will manufacture various products for the hospitals. The idea of a single laundry for all of the hospitals was adopted after a cost analysis that indicated a saving of thousands of dollars annually. The savings from a single central laundry instead of 10 small laundries will amount to 3.4 cents a pound in payroll alone, 2.5 cents after transportation. Four 16 ton trailer trucks are expected to transport laundry, pharmaceuticals, etc.,

on circuitous roads, servicing some hospitals every day, others on alternate days. Individual hospitals, however, will sterilize their own instruments, treatment trays, and similar items.

These hospitals will be open to all patients, although United Mine Workers Fund beneficiaries will have preference in case of bed shortage. Any qualified physician with patients in the area will have hospital privileges. Outpatient departments have been designed to be used as group practice offices. Dr. Warren F. Draper, executive medical officer of the fund, in an address at the ground-breaking ceremonies for the hospital at Man, W. Va., last October said:

"It has been the purpose of the Fund to utilize existing hospitals to the fullest extent possible. While there are some that provide a satisfactory quality of service at or near cost, there are others that supply an inferior quality of care often at exorbitant rates. . . .

"The inadequacy or total lack of hospital facilities in many of the coal mining areas remains for the most part unchanged.



Reading down from the top are architects' drawings of Whitesburg, Memorial Hospital, Whitesburg, Ky.; Beckley Central Hospital, Beckley, W. Va.; and Harlan Central Hospital, Harlan, Ky.

Many are privately owned and operated for profit. Their income is derived largely from beneficiaries of the Fund. Their facilities are usually denied to physicians other than those employed on their staffs. This discourages the needed number of competent physicians from locating in the areas and tends to create a monopoly. . . .

"In no instance will the combined number of beds in the new hospitals and the older hospitals be sufficient to meet all of the hospital needs of the people in these areas. The Fund will continue to pay the older hospitals for the care of its beneficiaries when the standards of service and rates are satisfactory. The miner may make his own choice under these conditions."

The report of the United Mine Workers of America Welfare and Retirement Fund for the year ending June 30, 1953, shows that hospital and medical care benefits of $56,444,329.78 were provided for 230,678 patients. Of these expenditures, 79% were for working miners and wives, children, and additional dependents; 8.4% were for disabled miners undergoing rehabilitation; 6.5% were for aged miners with pensions and their wives; 2.2% were for destitute and totally disabled miners; 3.9% were for widows and orphans.

The professional service of the fund is organized on the principle that responsibility for a medical care program rests entirely in medical hands. The executive medical officer and his associates have enlisted the cooperation of many leading physicians and medical organizations, including the Councils on Medical Service and Industrial Health of the A. M. A., in working out ways and means by which the standards of medical service to the miners and their families may be improved. In all of these coal mining states, liaison committees have been appointed by the state medical associations to advance the standards of medical care where needed, to develop good cooperative relationships between the practicing physician and the medical administrators of the fund, and to attempt to satisfactorily solve the problems that arise.

CORRECTIONS

Technicians for Overseas Assignments.—In THE JOURNAL, Feb. 13, 1954, page 606, in the item entitled "Technicians for Overseas Assignments," in the fourth and fifth lines, the words "Foreign Service Institute of the Department of State" should read "Foreign Operations Administration." The Foreign Operations Administration, which now has no organizational relationship with the Department of State, reports directly to the President.

Colorado State Medical Society.—In the item by this title in the Organization Section of THE JOURNAL, March 13, 1954, page 918, in the 12th line of the second paragraph the words "Code of Ethics" should have been "Code of Cooperation." The last paragraph of this item (on the next page) states that this society is currently constructing a $35,000 medical library building. This figure should have been $350,000.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.
1954 Annual Meeting, San Francisco, June 21-25.
1954 Clinical Meeting, Miami, Florida, Nov. 29-Dec. 2.
1955 Annual Meeting, Atlantic City, N. J., June 6-10.
1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.
1956 Annual Meeting, Chicago, June 11-15.

AERO MEDICAL ASSOCIATION, Hotel Statler, Washington, D. C., March 29-31. Dr. Thomas H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Mobile, April 15-17. Dr. Douglas L. Cannon, 537 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF NEUROLOGY, Shoreham Hotel, Washington, D. C., April 29-May 1. Dr. Alexander T. Ross, 1040 West Michigan St., Indianapolis 7, Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Hotel Galvez, Galveston, Texas, April 7-9. Dr. Normand L. Hoerr, 2109 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION, Webster Hall Hotel, Pittsburgh, May 14-15 Dr. Jack Matthews, 1617 Cathedral of Learning, University of Pittsburgh, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Hotel Taft, New Haven, Conn., May 6-8. Dr. Samuel X. Radbill, 7043 Elmwood Ave., Philadelphia 42, Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, Ambassador Hotel, Atlantic City, N. J, April 11-15. Dr. John Y. Sugg, 1300 York Ave., New York, Secretary.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Marlborough-Blenheim Hotel, Atlantic City, N. J., May 18-22. Dr. Neil A. Dayton, P. O. Box 96, Willimantic, Conn., Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, Philadelphia, Pa., April 8-10. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 6-8. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN ASSOCIATION FOR THE STUDY OF NEOPLASTIC DISEASES, Lord Baltimore Hotel, Baltimore, April 29-30. Dr. Bruce H. Sisler, P. O. Box 268, Gatlinburg, Tenn., Executive Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Sheraton-Mt. Royal Hotel, Montreal, Canada, May 3-5. Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif., Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Roney Plaza Hotel, Miami Beach, Fla., April 5-10. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Conrad Hilton Hotel, Chicago, April 5-9. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN DERMATOLOGICAL ASSOCIATION, The Greenbrier, White Sulphur Springs, W. Va., April 13-17. Dr. J. Lamar Callaway, Duke Hospital, Durham, N. C., Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 2. Dr. Lawrence E. Hinkle Jr., 525 East 68th St., New York 21, Secretary.

AMERICAN GOITER ASSOCIATION, The Somerset, Boston, April 29-May 1. Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., Secretary.

AMERICAN GYNECOLOGICAL SOCIETY, The Homestead, Hot Springs, Va., May 20-22. Dr. John I. Brewer, 104 South Michigan Blvd., Chicago, Secretary.

AMERICAN HEART ASSOCIATION, Conrad Hilton Hotel, Chicago, April 1-4. Dr. William H. Bunn, 44 East 23d St., New York 10, Secretary.

AMERICAN PEDIATRIC SOCIETY, The Inn, Buck Hill Falls, Pa., May 3-5. Dr. A. C. McGuinness, 237 Medical Laboratories, University of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN PHYSIOLOGICAL SOCIETY, Ambassador Hotel, Atlantic City, N. J., April 10-16. Dr. Milton O. Lee, 2101 Constitution Ave., Washington 25, D. C., Executive Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, St. Louis, May 3-7. Dr. R. Finley Gayle Jr., 6300 Three Chopt Road, Richmond 21, Va., Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, Atlantic City, N. J., April 12-16. Dr. Philip Handler, Duke University, Durham, N. C., Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Haddon Hall, Atlantic City, N. J., May 3. Dr. William M. M. Kirby, Univ. of Washington School of Medicine, Seattle 5, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, Atlantic City, N. J., April 12-16. Dr. Cyrus C. Erickson, 874 Union Ave., Memphis 3, Tenn., Secretary

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Washington, D. C., April 25-28 Dr. Casper M. Epsteen, 25 East Washington St., Chicago 2, Secretary.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Atlantic City, N. J., April 12-16. Dr. Carl C. Pfeiffer, 1853 West Polk St., Chicago 12, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF STERILITY, Roosevelt Hotel, New Orleans, May 13-15. Dr. Herbert H. Thomas, 920 South 19th St., Birmingham, Ala., Secretary.

AMERICAN SURGICAL ASSOCIATION, Hotel Cleveland, Cleveland, April 28-30. Dr. R. Kennedy Gilchrist, 59 East Madison St., Chicago 3, Secretary.

AMERICAN TRUDEAU SOCIETY, The Ambassador, Atlantic City, N. J., May 17-21. Dr. William G. Childress, 1790 Broadway, New York 19, Secretary.

ARIZONA MEDICAL ASSOCIATION, San Marcos Hotel, Chandler, April 25-28. Dr. Dermont W. Melick, 541 Security Bldg., Phoenix, Secretary.

ARKANSAS MEDICAL SOCIETY, Goldman Hotel, Fort Smith, April 19-21. Dr. J. J. Monfort, 215 Kelley Bldg., Fort Smith, Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Chalfonte-Haddon Hall, Atlantic City, N. J., May 4-5. Dr. W. Barry Wood Jr., 600 S. Kingshighway Blvd., St. Louis 10, Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Hotel Biltmore, Los Angeles, May 9-13. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

CATHOLIC HOSPITAL ASSOCIATION OF THE UNITED STATES AND CANADA, Atlantic City, N. J., May 17-20. Rev. John J. Flanagan, 1438 South Grand Blvd., St. Louis 4, Director.

CONFERENCE ON MICROCIRCULATORY PHYSIOLOGY AND PATHOLOGY, University of Texas, Galveston, Texas, April 8-9. Dr. Edward H. Bloch, Western Reserve University School of Medicine, Dept. of Anatomy, Cleveland 6, Chairman.

CONNECTICUT STATE MEDICAL SOCIETY, Bulkeley High School, Hartford, April 27-29. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Executive Secretary.

EASTERN SECTION, AMERICAN CONGRESS OF PHYSICAL MEDICINE, Newark, N. J., April 10. Dr. H. L. Rudolph, 400 North Fifth St., Reading, Pa., Secretary.

EASTERN STATES HEALTH EDUCATION CONFERENCE, New York Academy of Medicine, New York, April 29-30. Dr. Iago Galdston, 2 East 103d St., New York 19, Secretary.

FEDERATION OF AMERICAN SOCIETIES for EXPERIMENTAL BIOLOGY, Convention Hall, Atlantic City, N. J., April 12-16. Dr. M. O. Lee, 2101 Constitution Ave., Washington 25, D. C., Secretary.

FLORIDA MEDICAL ASSOCIATION, Hollywood Beach Hotel, Hollywood, April 25-28. Dr. Samuel M. Day, P. O. Box 1018, Jacksonville, Secretary.

GEORGIA, MEDICAL ASSOCIATION OF, Hotel Dempsey and Macon Auditorium, Macon, May 2-5. Dr. David H. Poer, 875 West Peachtree St. N.E., Atlanta, Secretary.

HAWAII MEDICAL ASSOCIATION, Maybel Smyth Bldg., Honolulu, May 13-16. Dr. Samuel L. Yee, 510 S. Beretania St., Honolulu 13, Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 18-21. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

INDUSTRIAL HEALTH CONFERENCE, Hotel Sherman, Chicago, April 24-30. Dr. E. C. Holmblad, 28 East Jackson Blvd., Chicago 4, Managing Director

INDUSTRIAL MEDICAL ASSOCIATION, Hotel Sherman, Chicago, April 27-30. Dr. Arthur K. Peterson, 28 East Jackson Blvd., Suite 1300, Chicago 4, Secretary.

IOWA STATE MEDICAL SOCIETY, Des Moines, April 25-28. Dr. Allan B. Phillips, 529 36th St., Des Moines 12, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 11-16. Dr. Eugene H. Dibble Jr., John A. Andrew Memorial Hospital, Tuskagee Institute, Ala., Secretary.

KANSAS MEDICAL SOCIETY, Hotel Jayhawk, Topeka, May 2-6. Dr. D. D. Vermillion, 315 West Fourth St., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Roosevelt Hotel, New Orleans, May 20-22. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 27-28. Dr. Everett S. Diggs, 1211 Cathedral St., Baltimore, Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 18-20. Dr. Robert W. Buck, 22 Fenway, Boston 15, Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Hotel Heidelberg, Jackson, May 11-13. Mr. R. B. Kennedy, 507 First Federal Bldg., Jackson, Executive Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, April 4-7. Dr. E. Royce Bohrer, 634 North Grand Blvd., St. Louis 3, Secretary.

NATIONAL CONFERENCE ON HEALTH IN COLLEGES, Hotel Statler, New York, May 5-8. Miss Charlotte V. Leach, 12th Floor, 1790 Broadway, New York 19, Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Ambassador, Chelsea and Ritz-Carlton Hotels, Atlantic City, N. J., May 17-21. Mr. Kemp D. Battle, 1790 Broadway, New York 19, Secretary.

NEBRASKA STATE MEDICAL ASSOCIATION, Hotel Cornhusker, Lincoln, May 10-13. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln 8, Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Haddon Hall, Atlantic City, May 16-19. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Hotel LaFonda, Santa Fe, May 13-15. Mr. R. R. Marshall, 221 West Central Ave., Albuquerque, Executive Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, New York, May 10-14. Dr. Walter P. Anderton, 386 Fourth Avenue, New York 16, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 3-5. Dr. Millard D. Hill, 203 Capital Club Bldg., Raleigh, Secretary.

NORTH DAKOTA STATE MEDICAL ASSOCIATION, Grand Forks, May 1-4. Mr. Lyle A. Limond, Box 1198, Bismarck, Executive Secretary.

OHIO STATE MEDICAL ASSOCIATION, Columbus, April 13-15. Mr. Charles S. Nelson, 79 East State St., Columbus 15, Executive Secretary.

OKLAHOMA STATE MEDICAL ASSOCIATION, Municipal Auditorium, Oklahoma City, May 9-12. Mr. R. H. Graham, 1227 Classen Drive, Oklahoma City, Executive Secretary.

PACIFIC NORTHWEST SOCIETY OF PATHOLOGISTS, Amphitheater, Dept. of Pathology, University of Washington School of Medicine, Seattle, April 23-24. Dr. John L. Whitaker, 315 South K St., Tacoma 3, Wash., Secretary.

PACIFIC NORTHWEST SOCIETY OF PLASTIC AND RECONSTRUCTIVE SURGEONS, Seattle, April 3. Dr. E. E. Banfield, Medical Arts Bldg., Tacoma 2, Wash., Secretary.

RHODE ISLAND MEDICAL SOCIETY, Rhode Island Medical Society Library, Providence, May 4-5. Dr. Thomas Perry Jr., 106 Francis St., Providence 3, Secretary.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:
MONTREAL, CANADA, Mount Royal Hotel, March 31-April 2. Dr. Harry S. Morton, 900 Sherbrooke St., West, Montreal, Canada, Chairman.

SOCIETY OF AMERICAN BACTERIOLOGISTS, William Penn Hotel, Pittsburgh, May 2-7. Dr. John Hays Bailey, Sterling-Winthrop Research Institute, Rensselaer, N. Y., Secretary.

SOCIETY OF NEUROLOGICAL SURGEONS, The Waldorf Astoria, New York, April 23-24. Dr. Edgar F. Fincher, Emory University, Ga., Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, Buck Hill Falls Inn, Buck Hill Falls, Pa., May 4-6. Dr. Sydney S. Gellis, 330 Brookline Ave., Boston 15, Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Ocean Forest Hotel, Myrtle Beach, May 11-13. Dr. Robert Wilson, 165 Rutledge Ave., Charleston, Secretary.

SOUTH DAKOTA STATE MEDICAL ASSOCIATION, Marvin Hughitt Hotel, Huron, May 18-20. Mr. J. C. Foster, 300 First National Bank Bldg., Sioux Falls, Secretary.

SOUTHWEST ALLERGY FORUM, Roosevelt Hotel, New Orleans, May 9-11. Dr. Stanley Cohen, S. W. Allergy Forum, 1441 Delachaise St., New Orleans 15, Secretary.

STUDENT AMERICAN MEDICAL ASSOCIATION, Sherman Hotel, Chicago, May 1-3. Mr. Russell F. Staudacher, 535 N. Dearborn St., Chicago 10, Executive Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Nashville, April 18-21. Mr. V. O. Foster, 706 Church St., Nashville 3, Executive Secretary.

TEXAS MEDICAL ASSOCIATION, Gunter Hotel, San Antonio, May 3-5. Dr. J. M. Travis Sr., 1801 Lamar Blvd., Austin, Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Albuquerque, N. Mex., April 6-9. Sidney B. Clark, 314 U. S. Court House, El Paso, Texas, Secretary.

WESTERN BRANCH, AMERICAN PUBLIC HEALTH ASSOCIATION, Olympic Hotel, Seattle, May 9-12. Mrs. L. Amy Darter, Division of Laboratories, State Dept. of Public Health, Berkeley, Calif., Secretary.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, Hotel Biltmore, Los Angeles, May 8. Dr. Edward J. Zaik, 740 S. Olive St., Los Angeles 14, Secretary.

FOREIGN AND INTERNATIONAL

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, Leeds, England, May 13-15, 1954. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Honorary Secretary.

BRITISH MEDICAL ASSOCIATION, Glasgow, Scotland, July 1-9, 1954. Dr. A. Macrae, B.M.A. House, Tavistock Square, London, W.C.1, England, Secretary.

CANADIAN MEDICAL ASSOCIATION, Vancouver, B. C., Canada, June 14-18, 1954. Dr. T. C. Routley, 244 St. George St., Toronto 5, Ontario, Canada, General Secretary.

CONFERENCE OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, Madrid, Spain, Sept. 26-Oct. 2, 1954. Secretariat, Escuela de Tisiologia, Ciudad Universitaria, Madrid, Spain.

CONGRESS OF INTERNATIONAL ASSOCIATION FOR THE PREVENTION OF BLINDNESS, New York, N. Y., U. S. A., Sept. 12-17, 1954. Professor Franceschetti, 2 Avenue Mirmot, Geneva, Switzerland, Secretary-General.

CONGRESS OF INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE BRONCHI, Geneva, Switzerland, June 5-6, 1954. Professor A. Montandon, Clinique Universitarie d O.R.L., Hôpital Cantonal, Geneva, Switzerland, Chairman.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Edinburgh, Scotland, July 9-10, 1954. For information address: Mr. A. J. Slessor, Department of Surgery, University New Building, Edinburgh 8, Scotland.

HEALTH CONGRESS OF THE ROYAL SANITARY INSTITUTE, Scarborough, England, April 27-30, 1954. Mr. P. Arthur Wells, Royal Sanitary Institute, 90 Buckingham Palace Road, London, S.W.1, England, Secretary.

INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Los Angeles, Calif., U. S. A., Oct. 10-14, 1954. For information write: Dr. T. H. Seldon, 102-110 Second Avenue S.W., Rochester, Minn., U. S. A.

INTERNATIONAL CANCER CONGRESS, Sao Paulo, Brazil, July 23-29, 1954. Prof. A. Prudente, 171 rua Benjamin Constante, Sao Paulo, Brazil, President.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 20-24, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Dr. Robert A. Moore, Washington University School of Medicine, St. Louis 10, Mo., U. S. A., Chairman, Committee on Arrangements.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Barcelona, Spain, Oct. 4-8, 1954. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Ill., U. S. A., Executive Secretary.

INTERNATIONAL CONGRESS ON GROUP PSYCHOTHERAPY, Toronto, Ont., Canada, Aug. 12-14, 1954. Dr. J. L. Moreno, Room 327, 101 Park Ave., New York 17, N. Y., U. S. A., Director of Organizing Committee.

INTERNATIONAL CONGRESS ON GYNECOLOGY AND OBSTETRICS, Geneva, Switzerland, July 26-31, 1954. Dr. H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland, President.

INTERNATIONAL CONGRESS OF HEMATOLOGY, Paris, Sept. 6-11, 1954. Dr. Jean Bernard, 86 rue d'Assas, Paris 6e, France, Secretary.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Rome and Salerno, Italy, Sept. 13-20, 1954. For information write: Segreteria XIV Congresso Internazionale di Storia della Medicina, Instituto di Storia della Medicine, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF HYDROCLIMATISM AND THALASSOTHERAPY, Opatija, Yugoslavia, May 8-13, 1954. Prof. C. Plavsic, Zeleni venac 1, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESS OF INDUSTRIAL MEDICINE, Naples, Italy, Sept. 13-19, 1954. Professor Scipione Caccuri, Director, Institute of Industrial Medicine Policlinico, Naples, Italy, Chairman, Organizing Committee.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Stockholm, Sweden, Sept. 15-18, 1954. Professor Anders Kristenson, Karolinska Sjukhuset, Stockholm 60, Sweden, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, São Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Ill., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY, Buenos Aires, Argentine, April 21-28, 1954. Direcion General de Sanidad Militar, Pozos 2045, Buenos Aires, Argentine.

INTERNATIONAL CONGRESS OF NUTRITION, Amsterdam, Netherlands, Sept. 13-17, 1954. Dr. M. van Eekelen, Centraal Instituut voor Voedingsonderzoek T.N.O., 61 Catharynesingel, Utrecht, Netherlands, General Secretary.

INTERNATIONAL CONGRESS OF OPHTHALMOLOGY, University of Montreal and McGill University, Montreal, Canada, Sept. 9-11, 1954, and Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 12-17, 1954. Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minn., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF ORTHOPEDIC SURGERY AND TRAUMATOLOGY, Berne, Switzerland, Aug. 30-Sept. 3, 1954. For information write: Professor M. Dubois, Isle-Hospital, Berne, Switzerland.

INTERNATIONAL CONGRESS OF PSYCHOLOGY, Montreal, Canada, June 7-12, 1954. For information write: Prof. H. S. Langfeld, International Union of Scientific Psychology, Eno Hall, Princeton University, Princeton, N. J., U. S. A.

INTERNATIONAL CONGRESS FOR PSYCHOTHERAPY, Zurich, Switzerland, July 21-24, 1954. Dr. H. K. Fierz, Theaterstrasse 12, Zurich 1, Switzerland, Secretary General.

INTERNATIONAL CONGRESS OF THE SOCIEDAD DE MÉDICOS INTERNOS, Residentes y Becarios del Instituto Nacional de Cardiologia de Mexico, Acapulco, Mexico, April 21-24, 1954. For information address: Dr. Jorge Soberón Acevedo, Avenida, Cuauhtemoc No. 300, Mexico, D. F., Mexico.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL INSTITUTE ON CHILD PSYCHIATRY, Toronto, Canada, Aug. 13-14, 1954. Miss Helen Speyer, International Association for Child Psychiatry, 1790 Broadway, New York 19, N. Y., U. S. A., Executive Officer.

INTERNATIONAL POLIOMYELITIS CONGRESS, Rome, Italy, Sept. 6-10, 1954. Mr. Stanley E. Henwood, 120 Broadway, New York 5, N. Y., U. S. A., Executive Secretary.

INTERNATIONAL SOCIETY OF ANGIOLOGY, North American Chapter, Hotel Mark Hopkins, San Francisco, Calif., U. S. A., June 19, 1954. Dr. Henry Haimovici, 105 East 90th St., New York, N. Y., U. S. A., Secretary.

INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION, Paris, France, Sept. 12-19, 1954. For information write: Colonel Julliard, Société Internationale de Transfusion Sanguine, 53 Boulevard Diderot, Paris 12e, France.

INTERNATIONAL SOCIETY FOR CELL BIOLOGY, Leiden, Netherlands, Sept. 2-9, 1954. Professor Peter J. Gaillard, University of Leiden, Leiden, Netherlands, Secretary.

INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Professor Fred C. Roulet, Hebelstrasse 24, Basle, Switzerland, Secretary-General.

IRISH MEDICAL ASSOCIATION, Killarney, Ireland, July 7-10, 1954. Dr. P. J. Delaney, 10, Fitzwilliam Place, Dublin, Ireland, Medical Secretary.

JOURNEES MEDICALES, Paris, France, April 21-25, 1954. For information write: Secretariat of the Journees, 12, rue Pierre-Geofroix, Colombes (Seine) France.

LATIN AMERICAN CONGRESS ON GYNECOLOGY AND OBSTETRICS, Sao Paulo, Brazil, July 10-15, 1954. Prof. Dr. Jairo Ramos, av. Brigaderio Luiz Antonio, 278-8° andar, Sao Paulo, Brazil, Chairman of Organizing Committee of Medical Congresses.

LATIN AMERICAN CONGRESS ON MENTAL HEALTH, Sao Paulo, Brazil, July 17-22. For information address: Professor A. C. Pacheco e Silva, Avenida Brigadeiro Luiz Antonio 651, Sao Paulo, Brazil.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION CONGRESS, Lake Garda, Italy, Sept. 15-21, 1954. Dr. Ada Chree Reid, 118 Riverside Drive, New York 24, N. Y., U. S. A., President.

PAN AMERICAN CONGRESS OF CHILD WELFARE AND PEDIATRICS, Sao Paulo, Brazil, July 15-21, 1954. For information address: Dr. Jairo Ramos, Avenida Brigaderio Luiz Antonio 278-8° andar, Sao Paulo, Brazil.

PAN AMERICAN CONGRESS OF GASTROENTEROLOGY, Sao Paulo, Brazil, July 19-24, 1954. For information address: Dr. Jairo Ramos, Avenida Brigadeiro Luiz Antonio 278-8° andar, Sao Paulo, Brazil.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY (Interim), São Paulo, Brazil, June 17-21, 1954. Dr. Moacyr E. Alvaro, Consolacao 1151, São Paulo, Brazil, President.

PAN AMERICAN CONGRESS OF VETERINARY MEDICINE, Sao Paulo, Brazil, April 3-10, 1954. Dr. Joao Soares Veiga, Rua Pires da Mota 159, Sao Paulo, Brazil, Chairman of Organizing Committee

PAN-PACIFIC SURGICAL CONGRESS, Honolulu, Hawaii, Oct. 7-18, 1954. Dr. F. J. Pinkerton, Suite 7, Young Bldg., Honolulu 13, Hawaii, Director General.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, London, England, May 17-19, 1954. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Ill., U. S. A., Secretary.

SOUTH AMERICAN CONGRESS OF ANGIOLOGY, Sao Paulo, Brazil, July 1954. For information write: Dr. Rubens Carlos Mayall, Rua Senador Vergueiro 73, Rio de Janeiro, Brazil, S. A.

WORLD CONGRESS OF CARDIOLOGY, Washington, D. C., U. S. A., Sept. 12-18, 1954. Dr. L. W. Gorham, 44 East 23d St., New York 10, N. Y., U. S. A., Secretary-General.

WORLD CONGRESS OF INTERNATIONAL SOCIETY FOR THE WELFARE OF CRIPPLES, Scheveningen-The Hague, Netherlands, Sept. 13-17, 1954. Secretariat: Miss H. P. Post, Pieter Lastmarkade 37, Amsterdam Z, Netherlands.

WORLD FEDERATION OF OCCUPATIONAL THERAPISTS, Edinburgh, Scotland, August 17, 1954.

WORLD MEDICAL ASSOCIATION, Rome, Italy, Sept. 26-Oct. 2, 1954. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary-General.

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various Centers, July 16. Final date for filing applications was Jan 16. Sec., Dr. Curtiss B. Hickox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Various centers, Sept. 2. *Oral.* Ann Arbor, Oct. 15-18. To be eligible candidates must have completed thirty-six months of training by October 1. Final date for filing application is May 1. Exec. Sec., Miss Janet Newkirk, 129 E. 52nd St., New York 22.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* Chicago, April 1-3 (candidates in the midwest). Los Angeles, June 15-17 (candidates west of the Rocky Mountains and west coast). The closing date for acceptance of applications for Chicago and Los Angeles was Feb. 1. New York, Sept. 22-24 (candidates on the east coast). The closing date for acceptance of applications will be April 1. *Written.* Oct. 18. Final date for acceptance of applications will be May 1. *Subspecialties. Cardiovascular Disease.* Chicago, April 1. *Gastroenterology.* Chicago, April 2-3. The closing date for acceptance of applications for the subspecialties was Jan. 15. Exec. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June. Final date for filing application was Jan. 15. Sec., Dr. Leonard T. Furlow, 600 S. Kingshighway, St. Louis 10.

AMERICAN BOARD OF NEUROLOGY AND PSYCHIATRY: *Psychiatry and Neurology.* Chicago, April 29-30. Final date for filing application was Feb. 1. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part II.* Chicago, May 10-17. Final date for filing application is April 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Practical examinations, 1954.* San Francisco, June 25-29; New York City, Dec. 5-9. Final date for filing applications was July 1, 1953. *Written, 1955.* Various cities, Jan. 24-25. Final date for filing application is July 1, 1954. *Practical examinations, 1955.* Philadelphia, June 10-15; Chicago, Oct. 9-14. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* St. Louis, Charlottesville, Va. and probably San Francisco, April 16-17. Sec., Dr. Harold A. Sofield, 122 South Michigan Ave., Chicago 3, Ill.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Boston, May 17-21. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: San Francisco, June 17-19. Sec., Dr. William B. Wartman, 303 E. Chicago Ave., Chicago 11.

AMERICAN BOARD OF PEDIATRICS: *Oral.* New York City, April 30-May 2; San Francisco, June 25-27; Chicago, Oct. 8-10 and New Haven, December.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION. *Oral and Written.* Washington, D. C., Sept. 5-6. Final date for filing applications is March 31. Sec., Dr. Earl C. Elkins, 30 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PLASTIC SURGERY: *Entire Examination.* Galveston, April 17-19. Final date for receipt of case reports was Jan. 1. Final date for receipt of case reports for the fall 1954 examination is June 1, 1954. Corres. Sec., Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PROCTOLOGY: *Part I.* Kansas City, Philadelphia and San Francisco, May 8. Sec., Dr. Louis A. Buie, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 13-14; New Orleans, Feb. 28-March 1, 1955; San Francisco, Mid-October, 1955; New York City, December, 1955. Sec., Dr. David A. Boyd, 102-110 Second Ave. S.W., Rochester, Minnesota.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Spring 1954. Final date for filing application was Dec. 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

DEATHS

Chapman, Eugene Rhea ⊕ Colonel, U. S. Army, retired, Los Angeles; born in Bennett, Ia., July 16, 1905; State University of Iowa College of Medicine, Iowa City, 1932; member of the State Medical Association of Texas; specialist certified by the American Board of Obstetrics and Gynecology; entered the regular army as a first lieutenant in December, 1934; served during World War II; promoted to major Jan. 8, 1946; retired as a colonel March 31, 1947; assistant dean and associate professor of obstetrics and gynecology, School of Medicine, University of California, Los Angeles branch since July 1, 1953; clinical professor of obstetrics and gynecology in the University of Texas Post-Graduate School, San Antonio branch, from September, 1950, to January, 1953; during this period of time was chief of the obstetric and gynecologic staff at the Nix Memorial and the Baptist Memorial hospitals, and also the Robert B. Green Memorial Hospital in San Antonio; died Jan. 21, aged 48, of glomerulonephritis.

Ingersoll, Edwin Stanley ⊕ Rochester, N. Y.; born in Lafayette, Ind., in 1886; Cornell University Medical College, New York, 1912; specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; chief surgeon, Rochester Dental Dispensary; consultant in otolaryngology, University of Rochester School of Medicine and Dentistry, Rochester General, Strong Memorial-Rochester Municipal, Genesee, and Rochester State hospitals in Rochester, and Frederick Ferris Thompson Hospital, Canandaigua; died in Brighton Jan. 8, aged 67, of myocardial infarction.

Kilgore, George Lester ⊕ San Diego, Calif.; born in 1902; Emory University School of Medicine, 1926; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Pacific Coast Oto-Ophthalmological Society; formerly a fellow in pathology at the Mayo Foundation in Rochester, Minn., where he changed to otolaryngology and rhinology, and ophthalmology; served during World War II; affiliated with San Diego County General Hospital and the Mercy Hospital, where he died Jan. 13, aged 51, of carcinoma of the pancreas.

Siever, Charles Moses ⊕ Topeka, Kan.; born in Maysville, W. Va., Sept. 1, 1874; Dallas (Tex.) Medical College, 1903; University of Kansas School of Medicine, Kansas City, 1907; an Associate Fellow of the American Medical Association; a captain in the medical corps of the Kansas National Guard from 1914 until 1918; served on the Mexican border and during World War I; resigned in 1935 after serving 19 years as head of the student health department at Kansas State College in Manhattan; at one time practiced in Holton, where for six years he was county health officer; died Jan. 15, aged 79, of acute congestive heart failure.

Kahle, Pierre Jorda ⊕ New Orleans; born in New Orleans Nov. 25, 1882; Medical Department of Tulane University of Louisiana, New Orleans, 1905; retired Sept. 23, 1953, after many years as professor and head of the department of urology at Louisiana State University School of Medicine; member of the Southeastern Surgical Congress and the American Urological Association; fellow of the American College of Surgeons; on the staffs of the Charity Hospital of Louisiana and Southern Baptist Hospital; died in Touro Infirmary Dec. 22, aged 71, of a cerebral vascular accident.

Dalton, Raymond Julian Aloysius ⊕ Key West, Fla.; born in Milwaukee July 9, 1895; Marquette University School of Medicine, Milwaukee, 1919; certified by the National Board of Medical Examiners; for many years practiced in Milwaukee, where he was assistant clinical professor of obstetrics and gynecology at his alma mater, and school board physician; in July, 1945 became Lake County health officer with headquarters in Tavares; left that position in July, 1947, to reenter the field of industrial medicine with the American Cyanamid Company at Brewster; in January, 1952, appointed Monroe County health officer, a position he held at the time of his death; died Jan. 18, aged 58, of acute coronary occlusion.

Brewer, Joel Runnels, Marlow, Okla.; Memphis (Tenn.) Hospital Medical College, 1908; died Jan. 15, aged 68, of pneumonia.

Brewster, H. W., Vimville, Miss.; University of Tennessee Medical Department, Nashville, 1890; died Jan. 17, aged 88.

Brown, Maynard O. ⊕ Cincinnati; Ohio State University College of Medicine, Columbus, 1929; died Jan. 14, aged 58, of a heart attack.

Charles, Robert LeRoy ⊕ Denver; Denver and Gross College of Medicine, 1904; member of the American Society of Anesthesiologists; affiliated with Childrens, St. Anthony, Denver General, and Colorado General hospitals, and St. Joseph's Hospital, where he died Dec. 12, aged 74, of myocardial infarction, posterior with cardiac rupture.

Crane, George Edward ⊕ Haverhill, Mass.; College of Physicians and Surgeons, Boston, 1913; for many years member of the board of health of Haverhill; affiliated with Hale Hospital; died Nov. 29, aged 80, of Banti's disease.

Daniel, Homer Melvin ⊕ Anderson, S. C.; Emory University School of Medicine, 1916; past president of the Anderson County Medical Society; affiliated with Anderson County Memorial Hospital; died in the Veterans Administration Hospital, Columbia, Jan. 14, aged 60, of cardiovascular renal disease.

Day, Jonathan Raynor ⊕ Claysville, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1903; died in the Presbyterian Hospital, Pittsburgh, Jan. 9, aged 82, of pyonephrosis and arteriosclerotic heart disease.

Eaton, Frederick George ⊕ Saratoga Springs, N. Y.; Albany Medical College, 1915; fellow of the American College of Surgeons; served overseas during World War I; for many years county coroner; consulting surgeon, Benedict Memorial Hospital in Ballston Spa, and Corinth (N. Y.) Hospital; senior surgeon, Saratoga Hospital, where he died Jan. 21, aged 60, of bleeding peptic ulcer.

Edwards, James Albert, Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1907; died Jan. 23, aged 82.

Fairfax, Henry Reginald ⊕ Brookhaven, Miss.; Medical College of Virginia, Richmond, 1898; died Feb. 16, aged 78.

Farrish, Robert Cyrus ⊕ Sherburn, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1901; went to the Mayo Clinic, Rochester, in September, 1901, and was assigned to surgical service at St. Mary's Hospital; left the clinic in July, 1902, to establish a general practice in Sherburn; in 1930 vice-president of the Minnesota State Medical Association; died Dec. 11, aged 86.

Fisher, George Carl ⊕ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1899; formerly on the faculty of Northwestern University Medical School; died Feb. 23, aged 80, of arteriosclerotic heart disease.

Floyd, Francis Patton, Alexandria, Va.; College of Physicians and Surgeons, Baltimore, 1914; died in Alexandria Hospital Nov. 24, aged 71, of peritonitis and perforated peptic ulcer.

Golden, Frank Patrick, Chadron, Neb.; John A. Creighton Medical College, Omaha, 1914; died Nov. 29, aged 72, of carcinoma of the stomach.

Green, Donarell R., Atlanta, Ga.; Howard University College of Medicine, Washington, D. C., 1893; died Dec. 26, aged 89, of uremia.

⊕ Indicates Member of the American Medical Association.

Harbison, James Edgar ⊕ Oklahoma City, Okla.; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1901; fellow of the American College of Surgeons; from 1923 to 1947 president of the Oklahoma City General Hospital; chief surgeon, Oklahoma Railway Company; division surgeon, Chicago, Rock Island and Pacific Railway Company; died Jan. 5, aged 76, of coronary occlusion.

Hays, Clarence Albert, Boston; Tufts College Medical School, Boston, 1922; died Jan. 1, aged 61.

Herzer, E. Faubel, McAllen, Texas; University of Louisville (Ky.) Medical Department, 1919; at one time practiced in Louisville, Ky.; died Jan. 13, aged 59, of coronary thrombosis.

Hickey, Joseph Garrett ⊕ Bywood, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1911; emeritus professor of physiology at Temple University School of Medicine, Philadelphia; died Jan. 20, aged 78, of coronary thrombosis.

Jacobson, T. LeRoy ⊕ Delavan, Wis.; Rush Medical College, Chicago, 1919; associated with the Delavan Clinic; died Jan. 3, aged 62.

Johnson, Whedon ⊕ Sarasota, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1943; member of the Medical and Chirurgical Faculty of Maryland; certified by the National Board of Medical Examiners; served during World War II; died Dec. 19, aged 36, of a left hemothorax and fractured ribs due to a fall.

Kelley, Arthur H., Savannah, Mo.; Ensworth Medical College, St. Joseph, 1907; died in Missouri Methodist Hospital, St. Joseph, Dec. 27, aged 69.

Kingsbury, William Neave, Reno, Nev.; L. R. C. P., London, M. R. C. S., England, 1904; affiliated with Washoe Medical Center and St. Mary's Hospital, where he died Feb. 1, aged 72, of acute myocarditis, emphysema, bronchiectasis, and probable cancer of the right lung.

Lawson, Esley Elwood, Medford, Okla.; Maryland Medical College, Baltimore, 1902; served during World War I; affiliated with Enid (Okla.) General Hospital; died in Enid Jan 12, aged 77, of cerebral hemorrhage, hypertension, and arteriosclerosis.

McDowell, Guy Marshall, Bay City, Mich.; Ohio Medical University, Columbus, 1906; past president of the Bay County Medical Society; for many years on the staff of the Michigan State Sanatorium in Howell; served on the staff of the Mercy Hospital, where he died Jan. 7, aged 73, of shock from injuries caused by a fall.

McQueen, Joseph Pickens ⊕ Birmingham, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; died in Jefferson Hillman Hospital Jan. 16, aged 65, of chronic myelogenous leukemia.

Marshall, Alexander George ⊕ El Paso, Texas; University of Illinois College of Medicine, Chicago, 1927; died in Indio, Calif., Dec. 25, aged 50, of injuries received in an automobile accident.

Mercer, John A., Greenfield, Ohio; Kentucky School of Medicine, Louisville, 1888; died in Washington C. H., Jan. 20, aged 87.

Philip, Albert ⊕ New York City; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1911; specialist certified by the American Board of Obstetrics and Gynecology; founder and past president of the American Hungarian Medical Association; member of the American Psychosomatic Society; formerly on the faculty of New York Homeopathic Medical College and Flower Hospital; served on the staff of Metropolitan Hospital; died Jan. 24, aged 66, of a heart attack.

Pond, Darwin Brayton ⊕ Chicago; Chicago College of Medicine and Surgery, 1907; fellow of the American College of Surgeons; in 1945 member of the House of Delegates of the American Medical Association; formerly a trustee of the Chicago Medical Society; fellow of the American College of Surgeons; served during World War I; on the staff of the Ravenswood Hospital; died Feb. 9, aged 74.

Quay, Russell Arthur ⊕ Stanford, Ill.; Northwestern University Medical School, Chicago, 1946; served during World War II; affiliated with Brokaw Hospital in Normal and Mennonite Hospital in Bloomington; died in St. Joseph's Hospital, Bloomington, Jan. 3, aged 37, of bulbar poliomyelitis.

Raisbeck, Alden ⊕ Lexington, Ky.; Cornell University Medical College, New York, 1943; member of the Illinois State Medical Society; interned at the Boston City Hospital in Boston; at one time a resident in psychiatry at the Illinois Neuropsychiatric Institute in Chicago; served during World War II; died Jan. 6, aged 35, of injuries received in an automobile accident.

Reaves, Lovett Martin ⊕ Dallas, Texas; University of Arkansas School of Medicine, Little Rock, 1929; served during World War II; affiliated with St. Paul's Hospital, where he died Jan. 2, aged 49, of multiple myeloma.

Rosenberg, Max ⊕ Long Island City, N. Y.; Julius-Maximilians-Universität Medizinische Fakultät, Wurzburg, Germany, 1921; died Nov. 16, aged 59, of a heart attack.

Schlumberger, Pierre Rhyner, Gibbon, Neb.; John A. Creighton Medical College, Omaha, 1917; died in Hastings, Jan. 1, aged 60, of myocardial infarction.

Scott, David Roscoe ⊕ Chicago; University Medical College of Kansas City, Mo., 1911; on the staff of the Norwegian American Hospital; served during World War I; died Feb. 5, aged 68, of acute coronary occlusion.

Settle, James Albert ⊕ Hutchinson, Kan.; University Medical College of Kansas City, Mo., 1893; served during World War I; died in the Grace Hospital Jan. 23, aged 84.

Seybold, Nicholas Joseph ⊕ Toledo, Ohio; Toledo Medical College, 1913; served during World War I; affiliated with Maumee Valley Hospital, Toledo State Hospital, and St. Vincent's Hospital, where he died Jan. 21, aged 63, of melanosarcoma.

Shaw, Rowell Wilbur ⊕ Gilbertown, Ala.; Memphis (Tenn.) Hospital Medical College, 1900; died in Butler Jan. 12, aged 78, of sarcomatosis.

Slavin, Albert, Boston; Middlesex College of Medicine and Surgery, Cambridge, Mass., 1927; served during World War II; died in the Boston City Hospital Jan. 11, aged 53.

Smith, Max Truman, Carmel, Calif.; Jefferson Medical College of Philadelphia, 1906; fellow of the American College of Surgeons; past president of the Idaho State Medical Association; died Dec. 31, aged 71, of coronary occlusion.

Taylor, Ernest R., Minneapolis; College of Physicians and Surgeons, Medical Department of the Kansas City University, Kansas City, Kan., 1896; died in St. Peter (Minn.) State Hospital Dec. 17, aged 80, of senility.

Templeton, Allan Alexander, Highland Park, Mich.; Dearborn Medical College, Chicago, 1905; served as president of the Peoples Federal Savings and Loan Association in Detroit; died Feb. 17, aged 79, of coronary occlusion.

Thayer, Alfred Edward, Mobile, Ala.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1884; died Nov. 24, aged 90.

Thompson, Fred F. T. ⊕ The Dalles, Ore.; University of Oregon Medical School, Portland, 1906; served as mayor; affiliated with The Dalles General Hospital; died Jan. 7, aged 71, of cerebral hemorrhage.

Tyler, Winsor Marrett ⊕ Brookline, Mass.; Harvard Medical School, Boston, 1903; served during World War I; medical examiner for Middlesex County; died in Beth Israel Hospital in Boston, Jan. 9, aged 77, of pneumonia.

Wilson, John G., New Hampton, Mo.; Marion-Sims College of Medicine, St. Louis, 1900; died Nov. 29, aged 80.

Wilson, Luther Elgin, Birmingham, Ala.; University of Pennsylvania School of Medicine, Philadelphia, 1911; died Dec. 16, aged 70, of cerebral vascular accident.

Witham, Albert Arthur, Portland, Ore.; University of Oregon Medical School, Portland, 1896; served on the staff of Emanuel Hospital; died Jan. 26, aged 86, of arteriosclerosis.

GOVERNMENT SERVICES

ARMY

Award to Colonel Halloran.—A bronze plaque in memory of the late Col. Roy D. Halloran, M. C., was recently unveiled at the Walter Reed Army Medical Center, Washington, D. C., and the Army's Certificate of Achievement was awarded to him posthumously. The plaque, donated by the American Psychiatric Association, was presented by Dr. Winfred Overholser, superintendent of St. Elizabeth's Hospital, Washington, D. C., to Major Gen. Leonard D. Heaton, M. C., commanding general of the center. The certificate, which was presented by Major Gen. George E. Armstrong, Surgeon General, to Colonel Halloran's son and daughter, credits Colonel Halloran with establishing the groundwork for the Army's present-day psychiatric program. He died at his desk on Nov. 10, 1943, while on duty in the Office of the Surgeon General.

A. M. A. Service for Service Men.—The *U. S. Armed Forces Medical Journal* has inaugurated a series of articles entitled "A Message from the A. M. A." to meet the need for closer communication between organized medicine and the physician in uniform. The series was introduced in the January issue by Dr. Edward J. McCormick, President of the Association, who explained that each month the Council on National Emergency Medical Service would outline one of its projects, present a subject of current interest to physicians in uniform, or answer questions that have been submitted. The items discussed will depend on the nature of inquiries currently being received by the Council. Such inquiries should be addressed to the Council on National Emergency Medical Service, American Medical Association, 535 N. Dearborn St., Chicago 10.

AIR FORCE

Medical Unit Receives Commendation.—Personnel of the 5005th Air Force Hospital located at Elmendorf Air Force Base, Alaska, have been commended by the Surgeon General for their devotion to duty during a fire in the early morning of Feb. 3. Major Gen. Harry G. Armstrong, Surgeon General, was at Elmendorf Air Force Base during the fire on a tour of inspection. The commendation stated: "The existing emergency plan was promptly implemented, and in a rapid and orderly manner, the evacuation of approximately 200 patients was accomplished. At all times, the safety of the patients was uppermost in your minds." General Armstrong further stated: "The true test of the ability of any organization and its leaders in their capability to perform effectively in a dire emergency. You may well be proud to realize that your unit performed outstandingly in a situation which could have easily resulted in a major catastrophe. In my opinion, the 5005th USAF Hospital has demonstrated that it is without question one of the finest units of the USAF Medical Service. It is evident that yours is a unit of superb leadership, training, and discipline."

PUBLIC HEALTH SERVICE

Seminar on Milk Sanitation.—Milk-control authorities from five states and the District of Columbia and milk and food experts of the armed services recently held a five-day seminar on milk sanitation in Washington, D. C. The seminar was conducted by the Public Health Service. The subjects discussed included bulk-milk tanks, farm water supplies, vat-type milk plants, the new State-Federal Interstate Milk Shippers' Certification Program, and methods of testing new kinds of equipment.

The seminar was conducted by Mr. Darold W. Taylor, Regional Milk and Food Consultant, Washington, D. C., and Mr. Hugh E. Eagan, Educational Specialist, Public Health Service Communicable Disease Center, Atlanta, Ga. This was one of a series of monthly seminars on subjects relating to public health. The next seminar will be held in February and will deal with the prevention of home accidents.

VETERANS ADMINISTRATION

Survey of Trained Manpower.—In a research study, released Feb. 10, the Veterans Administration found that 7,800,000 veterans had received GI Bill training since the program began in June, 1944. This total represents more than half of all veterans who served in World War II.

According to the study 1,500,000 studied for the professions, and of these 180,000 studied medicine and related courses; 113,000 veterans chose physics, biology, chemistry, geology, metallurgy, and other courses. Of the 2,600,000 craftsmen who learned their skills under the GI Bill, the largest proportion, 711,000, or 38%, studied mechanics; automobile mechanics was most popular, and aircraft mechanics was second. Television and radio trainees numbered 438,000, construction workers (carpenters, bricklayers, plumbers, and others) totaled 383,000, metalworkers, 288,000, electricians, 138,000, and refrigeration and air conditioning mechanics, 116,000.

A total of 238,000 schoolteachers, 243,000 accountants, 107,000 lawyers, 93,000 social scientists, 17,000 writers and journalists, 4,000 social workers, 1,500 librarians, and 36,000 students of the ministry, representing all major faiths, were trained under the GI Bill.

Other types of GI Bill training taken by veterans include: art and design, nearly 210,000 veterans; barbers and beauty culturists, 83,000; policemen and firemen, 43,000; bakers and meat cutters, 45,000; dressmakers and tailors, 76,000; shoemakers, 32,000; upholsters, 55,000; music students, 62,000; embalmers and undertakers, 9,000; surveyors, 4,000; and printers, engravers, and typesetters, 61,000. The VA survey further disclosed that of the 7,800,000 World War II veterans who had taken GI training, more than 2,000,000 had gone to college. Although training under the World War II GI Bill will not expire until 1956, new enrollments for practically all veterans came to an end in July, 1951, the deadline for starting training for the majority of veterans.

Residencies in Psychiatry.—The Veterans Administration Hospital, Lyons, N. J., has available residencies in psychiatry for a one-to-three-year period that are fully accredited by the American Board of Psychiatry and Neurology. The training program consists of lectures, conferences, and seminars under the direction of the department of psychiatry, New York Medical College, and offers intensive training, both intramurally and through rotation in special hospitals and clinics in the adjacent area. There is also an extensive series of guest lecturers as well as an annual institute at the hospital. Training may commence at any time.——Residencies are available in the 88-bed psychiatric service of the new veterans' hospital in Chicago's West Side Medical Center. Visiting staff from faculties of three of Chicago's medical schools afford excellent opportunity for training in dynamically oriented psychotherapy, the somatic therapies, and neurology. Salaries for residents at this hospital are as follows: junior resident, $2,640 per annum; intermediate resident, $2,970 per annum; and senior resident, $3,300 per annum. Additional information can be obtained from H. H. Garner, M.D., Chairman, Sub-Committee on Psychiatry, Chicago Medical School, 710 S. Wolcott St., Chicago 12.

Vacancies at Oteen.—The Veterans Administration Hospital at Oteen, N. C., has several vacancies at present for physicians who are trained in diseases of the chest or who are interested in receiving training in that field.

FOREIGN LETTERS

ARGENTINA

Cardiac Syndrome in Trypanosomiasis.—The cardiac manifestations of trypanosomiasis were studied by Chagas and Laranja in Brazil and by Mazza, Romaña, Cossio, and Rojas in Argentina. A special symposium on the subject was held in 1953 in the Inter-American Congress of Cardiology in Buenos Aires. A special section has been organized in the Institute of Cardiology, Pabellon Inchauspe, of the Ramos Mejía Policlínico in Buenos Aires. The new section specializes in the diagnosis, treatment, and prophylaxis of the cardiovascular lesions and disturbances produced by trypanosomiasis. In a recent survey in Andalgalá Drs. C. Romaña and M. Kirschbaum found that 37% of the population were infected by Trypanosoma cruzi. The diagnosis was made by complement fixation reaction and xenodiagnosis. Of the positive cases 48% had abnormalities in the electrocardiogram. In the province of Córdoba, 47% of the Triatomas are infected by Trypanosoma cruzi. In a survey by Dr. C. M. Bettinotti reported in *Semana méd.*, page 98, 1954, the proportion of human beings infected was 24% in the province of Córdoba and 16.6% in the city of Córdoba.

Professional Colleges.—Twenty years ago Drs. Fidanza and Rubino organized the "Colegio de Médicos de la Provincia de Santa Fe" modelled after the French colleges of physicians. The college is elected by all the physicians of the province of Santa Fe. Its functions are control of professional ethics, regulation of professional fees, detection of illegal medical practices, and advising the government on medical problems. Recently a law has been proposed by which the college will be directed by a body consisting of two delegates of the government, one delegate of the General Confederation of Labor, and two delegates of a medical association affiliated to the same confederation. This proposal has been strongly opposed by the physicians of Santa Fe and by the Medical Confederation of the Argentine republic.

BELGIUM

Natal Mortality.—The National Society for Childhood in collaboration with the World Health Organization organized at Brussels in September, 1953 a congress for the study of natal mortality. The toxemias of pregnancy were studied by Janssens and Renaer. These conditions are characterized by one or several of the following symptoms: edema, proteinuria, hypertension, convulsions, and/or coma. They appear in almost 7% of all pregnant women, and 25% of maternal deaths are attributable to them. The prenatal and postnatal mortality is 7 to 10% for the nonconvulsive and 30% for the convulsive type; about 15% of stillbirths are due to this cause. Professor van Bouwdijk reported that from 1938 to 1951 in the Netherlands 164 cases of eclampsia resulted in 51 stillbirths (31.1%), and 143 cases of preeclampsia resulted in 44 stillbirths (30.7%). The stillbirth rate represented about 60% of the mortality among babies born after more than 34 weeks of gestation. The author believes that the fetal mortality due to toxemia of pregnancy can be reduced by early diagnosis and prompt treatment. The most important examination as far as toxemia of pregnancy is concerned is the regular reading of blood pressure and weekly weighing of the mother-to-be.

James Spence spoke on the organization of a hospital nursing service for premature infants, which was achieving good results, and stated that the following percentages of survival can be obtained: 20% for those under 1,000 gm.; 70% for those weighing 1,000 to 1,499 gm.; 90% for those weighing 1,500 to 1,999 gm.; and 98% for those weighing 2,000 to 2,500 gm. If an average of 6% of all births are premature and the birth rate is 15 to 20 per 1,000 per year, from 90 to 120 premature babies will be born each year in a town of 100,000 inhabitants. This would require six or seven hospital beds to provide only for babies weighing less than 2,000 gm. Cieters stressed the importance of close cooperation between the obstetrician and the pediatrician, particularly in the treatment of premature infants. He also studied the fetomaternal immunologic conflict and recommended that systematic determination of the Rh factor and checking for maternal isoimmunization be included in every prenatal examination. Lelong stated that infant mortality in the first month of life can be reduced by a fight against infection and closer attention to feeding problems. He stressed (1) the importance of the quality of living quarters; (2) the fact that the mother should have sufficient income to allow her to stay home for the three months following the birth of her child; and (3) the creation of specialized centers for hematological research, for the treatment of congenital malformations, and for premature babies. In Paris statistics based on more than 1,500 premature infants show that, if the three days are excepted, the mortality rate for babies born prematurely is not greater than that for babies born at term.

Malaria in Katanga.—At a meeting of the Belgian Society of Tropical Medicine, in October, Feuillat, Parent, Peeters, and Vincke reported on the recent advances made in the fight against malaria in Katanga. The government has staged a campaign against Anopheles mosquitoes by means of chlorophenothane (DDT). In the urban sections, malaria has been greatly reduced and the residual cases can be attributed to infections brought in from other areas. In the rural sections the results are encouraging but not as good as in the cities. The most important cause for this difference appears to be the fact that about 30% of the walls of rural dwellings were renewed following residual spraying with chlorophenothane. In some rural regions the use of chlorophenothane combined with the administration of Daraprim (2:4-diamino-5-[*p*-chlorphenyl]-6-ethyl pyrimidine) gave encouraging results. The introduction of malaria into zones protected by chlorophenothane was found to be due to workers and their families returning to the mines after a long vacation in their native villages. Consequently, it was necessary to fight this exogenous malaria by chemoprophylaxis, particularly with Daraprim.

Tuberculosis.—At a meeting of the Belgian Society of Tuberculosis, the problem of incurable tuberculous patients was discussed. Dwelshauwers stated that in 1951 in Belgian sanatoriums, persons with incurable disease occupied 6 to 35% of the beds and that the length of stay was six months to two years. For psychological reasons he does not advocate concentrating all patients with incurable disease in the same specialized establishment. He prefers either small groups of less than 30 patients or hospitalization of a small number in sanatoriums. These patients should not be treated at home unless it is impossible to place them elsewhere.

BRAZIL

Vaccination Against Tuberculosis.—A Brazilian method of antituberculous vaccination with large doses of BCG vaccine by mouth was reported by Dr. F. von Deinse in a paper published in *La semaine des hôpitaux*, Dec. 30, 1953. The author of the method is Dr. A. de Assis, who in 1945 proposed giving at birth three successive doses of 30 mg. each of BCG vaccine and thereafter five doses of 100 mg. each at monthly intervals. This new method was applied from February, 1945, to February, 1946, to 61 children who were living in a tuberculous environment and could be closely followed up till February, 1950.

The items in these letters are contributed by regular correspondents in the various foreign countries.

The results were so encouraging that the method was adopted and applied to all newborn infants exposed to contagion. In about one-third of those children subjected to this vaccination, the allergy for tuberculin tends to disappear. The method was then modified, and the infants were from the first given 100 mg. doses monthly until a total of 600 mg. had been given. This procedure was tested in one of the slums of Rio de Janeiro, and the mortality rate from tuberculosis in babies living in a tuberculous environment was reduced to 0.84%, whereas it was 3.13% in nonvaccinated babies. In São Paulo, J. Rosemberg, having noted the innocuousness of BCG vaccine given by mouth to tuberculous children and adults, introduced the "indiscriminate" method of vaccination without previous tuberculin testing. The dispensary of the Institute Clemente Ferreira in São Paulo has had excellent results with this method in the poorest districts where most babies live in contact with tuberculous patients. All newborn infants controlled by this dispensary are given six oral doses of 100 mg. each of BCG vaccine every 15 days from birth. All inhabitants under 20 years of age in the districts controlled by this dispensary are given three doses of 200 mg. of the vaccine by mouth without previous tuberculin testing. J. Rosemberg and co-workers have studied the tuberculin reactions in babies protected from any contagion after ingestion of one or several successive doses of 100 mg. of BCG vaccine. After a single dose, the tuberculin reaction does not always become positive but the Mitsuda reaction to lepromin always does. Repeated doses of the vaccine may cause the tuberculin reaction to disappear in children whose reaction had become positive as a consequence of the initial ingestion of 100 mg. of BCG vaccine, whereas the Mitsuda reaction is enhanced by repeated doses of the vaccine. Since 1951 an extensive campaign for oral BCG vaccination has been conducted in the state of São Paulo.

Use of Curare in Biliary Tract Operations.—In the Hospital das Clínicas of the Medical School of São Paulo, curare has been used since 1946. At first it was used as an auxiliary to the general anesthetic, and now it is used as the main anesthetic agent when the latter is given with nitrous oxide. Intermittent doses of curare are given when needed. Although the first method gave good results, the results are even better with the latter method, and the muscular relaxation, blood pressure level, and pulse stability induced are very satisfactory. Even patients in the poorest condition are able to tolerate the anesthesia and the operation better with this method than with other kinds of anesthesia. According to a paper published in *Revista paulista de medicina* (**43**:490 [Dec.] 1953) by Drs. R. Figueiredo, P. Bove, and J. Figliolini, in biliary tract operations the anesthetic agent should not modify the biliary physiology and should not damage the hepatic cells. The biliary diseases are frequently followed by functional disturbances of the sphincter of Oddi, which may be diagnosed by the operative cholangiomanometry. For this reason it is important to avoid all factors that might disturb the manometric measures and the cholangiograms. The authors found that curare given with nitrous oxide does not change biliary pressure or the cholangiographic aspect, if morphine or atropine is not given to the patient in the two or three hours preceding the operation. Because of this fact, curare is superior to spinal or regional anesthesia. In comparison with other kinds of anesthesia, the authors believe that curare and nitrous oxide is the combination best tolerated, least dangerous, and most likely to permit exact biliary manometry and easier cholangiography.

FINLAND

Throat Diseases and Chemotherapy.—Otolaryngological publications abound in dramatic accounts of isolated cases of throat disease ending in recovery after modern chemotherapy. What is much rarer is a comprehensive statistical study of such cases before and after the introduction of this treatment. Dr. Leo Ojala and Dr. Urpo Siirala have made such a study, basing it on the annual reports of seven large Scandinavian hospitals including the otolaryngological hospitals in Helsingfors and Aabo. Similar hospitals in Denmark, Norway, and Sweden have provided their quota, bringing the total of hospital-treated, otolaryngological patients up to 41,069. Three different periods were studied. The first (1931-1932) represented the prechemotherapy period. The second (1937-1938) represented a transitional period, with sulfonamides coming into vogue. The third (1950-1951), with a total of 21,410 patients, synchronized with the fairly universal standardization of modern chemotherapy. Throughout these periods the otolaryngological patients could be classed in three approximately equal groups having acute infectious diseases, chronic infectious diseases, and noninfectious diseases respectively. The decrease in mortality was greatest among the patients with acute infectious diseases. That there should also be a decrease in mortality in the noninfectious disease group may at first sight be surprising, but in four such cases the ultimate cause of death was a complicating infection.

Another effect of modern chemotherapy was a shortening of the duration of hospital treatment in the period under review by about 37%, but as there had been an increase in the number of hospital beds available in the same period, resulting in the admission of a greater number of light cases, this improvement could not exclusively be credited to modern treatment though it was assuredly the most important factor. This investigation, details of which with tables are published in *Nordisk medicin* for Oct. 22, 1953, also shows how the patients fared according as they suffered from acute otitis media, chronic otitis media, or sinusitis. In every form of disease there has been a fall in the mortality and complications, but the mortality from acute otitis showed a greater decline in Swedish than in Finnish hospitals, presumably because the hospital accommodation for such cases was better in Sweden.

ITALY

Segmental Enteritis.—The annual conventions of the Italian societies of medicine and surgery began in Rome, Oct. 14, 1953. They were held in the Aula Magna of the Città Universitaria with the participation of the High Commissary of public hygiene and public health and almost all Italian clinicians. Prof. Cesare Frugoni, University of Rome, reviewed the latest advances in internal medicine and general surgery. Segmental enteritis was discussed in a joint session of the two societies. Professor Antognetti, University of Genoa, and Dr. Zinolli reported on the medical aspect. According to them, segmental enteritis is a morbid process that may involve the entire intestine, in a segmental manner, with intercalated areas of healthy tissue of varying length. It is a morbid process of the granulomatous type and of unknown cause and obscure pathogenesis. It affects mainly the terminal ileum and has a chronic cicatricial course that produces stenosis. Sometimes acute episodes occur, and superimposed infection may lead to the formation of abscesses and fistulas. Differential diagnosis between the granulomatous type and ileocecal tuberculosis is sometimes difficult because giant cells are formed in both. It is, however, important to rule out ileocecal tuberculosis, sarcoidosis, syphilitic enteritis, and malignant granuloma. Some granulomatous inflammatory forms, such as the eosinophilic granuloma of the cecum and the granuloma of the plasma cells, are probably identical to segmental enteritis.

The acute form presents a complex of symptoms analogous to those of an acute intra-abdominal condition. The prognosis of the primary bacterial forms is very unfavorable; on the other hand, the nonbacterial forms may either regress spontaneously or become chronic. Signs of intestinal stenosis and fistulas are present in the chronic forms, in addition to signs of impairment of the general condition and an altered intestinal function. Although the treatment of choice is mainly surgical, some antibiotic and chemotherapeutic preparations may control, or at least modify, some phases or manifestations of the disease.

The surgical aspect of the subject was discussed by Professor Pettinary, University of Padua. He spoke against radical treatment of segmental enteritis and said that the aim of medical therapy is to put the intestine at rest by eliminating all the toxic and irritative factors, to decrease the virulence

of the intestinal bacteria and their toxins, to promote healing of the involved areas, to prevent the formation of new ones, and to combat diarrhea, pain, and loss of weight. Diet and rest are of proved value; cortisone and radiological therapy are being tried, but their results seem to be temporary and limited. Intestinal drainage with continuous aspiration by means of a Miller-Abbott tube may be beneficial, especially in acute and subacute forms and during the enteritic phase of the chronic forms.

Except for the phlegmonous forms, surgical treatment should never be used in the acute stage. If on opening the abdomen the diagnosis is found to be wrong, the intervention should be limited to a simple laparotomy, with or without removal of the appendix. Primary resection is accompanied by a high mortality rate, and the late results have not as yet been thoroughly evaluated. A vast primary resection (right hemicolectomy) is the operation of choice in the chronic phase, when a tendency toward the development of fibrosis is present. A two stage resection, with simple ileotransversostomy with exclusion, should be performed in the stage of development of the disease. Anastomosis in continuity should never be performed. Resection in continuity should be performed only when the segmental enteritis is not terminal. In every case the damaged segment should be resected beyond the lesion with awareness, especially in the case of reintervention, that these patients, whose intestinal absorption is greatly impaired, do not tolerate well a great loss of small intestine. Relapses occur in more than one-third of the patients even after several years. This may be due to failure to remove all the diseased bowel or to the formation of new lesions.

Although segmental enteritis tends to become localized, its evolution depends on general causes, and it often involves multiple areas. The problem of its treatment is far from solved. Surgery aims to remove the focus or to eliminate at least the zone that is most severely affected and to prevent the development of obstruction or fistulas. In any case it should be preceded by, accompanied by, and followed by continuous medical therapy.

Professor Vallebona, University of Genoa, discussed the radiological aspect. He pointed out the value of administering the contrast medium by mouth or through the rectum and stressed the advantages of divided doses of barium sulfate. He described the classic signs of segmental ileitis, namely, the presence of an ileal loop that is deformed, narrow, sometimes filiform, and fixed. He stated that the roentgenologist should not only ascertain the presence of an ulcerative hyperplastic ileitis but also determine its exact location, keeping in mind that more than one intestinal segment may be affected.

Meeting on Military Medicine.—The International Committee of Military Medicine and Pharmacy met in Rome, Oct. 14-18, 1953, with Dr. Jame, a general in the French Army, as chairman. The 16th meeting of the International Office of Documentation of Military Medicine was held at the same time. The honorary chairman of this meeting was the Italian minister of defense, and the acting chairman was Dr. Pera, a general in the Italian Army. Dr. Pera is also the director general of the Italian Medical Corps. Official representatives were sent by 33 nations and 5 international organizations including the World Health Organization, the Red Cross International Committee, and the World Medical Association. Dr. Voncken, who is a general in the Belgian Army and also the secretary-general of the Committee, discussed international medical law. It was agreed that the new procedures used to suppress political enemies and the new means of euthanasia for wounded and incurable persons should not be entrusted to any physician or military or national leader. With regard to whether the results of new discoveries in the field of atomic, biological, and chemical warfare should be made public by the authors, it was agreed that in some cases the results and oftener the means used to obtain them should be withheld. No dangerous or fatal experiment should be carried out on living human beings, particularly prisoners of war, persons wounded on the battle field, convicts, and persons in concentration camps. The physician should always respect the life of a human being, from his conception to his death, and should try to alleviate his suffering and prevent his death. The codification of international medical law to be approved by all nations was recommended.

LONDON

BCG Vaccination.—An analysis of the results obtained from BCG vaccination of 3,500 infants at St. Mary's Maternity Hospital, Manchester, during the last three years has been published by Prof. Wilfrid Gaisford and Margaret Griffiths (*Tubercle* **35:** 7, 1954). Initially, the recommendations of Walgren were followed: that newborn infants required twice the dose of older children and took twice as long to become tuberculin-positive and then produced such a reaction only when 1:100, or even 1:10, old tuberculin was used and that the thigh was the best site for vaccination. Following intradermal vaccination of 367 infants with 0.2 ml. of the Danish vaccine supplied by the Ministry of Health, all became tuberculin-positive, with satisfactory reactions at the site of inoculation. Within the next four to nine months, enlarged lymph nodes developed in 93 (25%) and in 53 resulted in abscess formation. Modifications in technique were then introduced until finally the dose was reduced to 0.05 ml. given as a single injection in one arm. The next 287 infants all became tuberculin-positive, and there was only one axillary abscess. Subsequently 68 infants were vaccinated with two injections of 0.05 ml., one in the arm and one in the thigh; inguinal abscess occurred in two and inguinal adenitis in 16 others, whereas no axillary abscess developed and only two infants had axillary adenitis. Since then all injections have been given in the arm.

An interesting feature of the complications, none of which were serious, was the complete freedom of the abscesses from secondary infection. All the infants gained weight satisfactorily, contrary to the reports that vaccinated infants gain weight more slowly. Two practical points are stressed: 1. The parents should be warned to tell their doctors which arm was used for the vaccination, because no injection should be given in this arm for six months; such injections may be followed by a flare-up at the site of inoculation and in the axillary gland. 2. The site chosen for BCG vaccination should not be above the insertion of the deltoid muscle; vaccination above this site may lead to involvement of the supraclavicular gland, which is part of the cervical chain that is always under a strain from upper respiratory infections.

Investigations showed that the low incidence of complications reported by Wallgren in spite of such relatively large doses was due to the fact that the Swedish vaccine was much more attenuated than the Danish. During the three years of this investigation there were no known cases of tuberculosis in vaccinated infants. There were 27 deaths, with necropsy in 9, and in none of these was there any evidence of spreading infection due to BCG. During the same period of time there were 17 recorded deaths from tuberculosis in Manchester in unvaccinated children under the age of 2 years. The final conclusion is as follows: "If vaccination is to be done, it should be done at the time it is most needed—namely earliest infancy —but that as the technique is by no means easy at this age except with trained help and considerable experience, it should be in the hands only of those competent as a result of such experience and should not be lightly recommended as a routine procedure in the newborn."

Loans for Group Practices.—The Minister of Health has accepted a recommendation that £100,000 should be set aside annually for the purpose of stimulating the formation of group practice, which is defined as follows: "Group practice applied to general medical practice means that the medical practice is carried on by several general practitioners working together in close association, consulting one another about their patients, and doing their 'surgery work' in whole or in part in a common building controlled by the doctors. All members of a 'group' should work in the common surgery premises even if on

occasions they also work at separate branch surgeries. A group practice should employ ancillary help to the extent of one or more persons who can provide services of the secretarial, nursing, receptionist, or almoner type. Normally, a group should consist of three, four, five or six. Larger numbers tend to diminish the value of group association. The group may or may not be a partnership, but if not, there must be a proper understanding between the members of a group on the sharing of the earnings of the group and particularly as to the sharing of expenses. Patients must continue to be the responsibility of the doctor of their choice in the group. The group should provide a twenty-four hours' service to patients and also proper off-duty and holiday relief for its members."

It has now been officially announced that this sum shall be expended in the form of interest-free loans, which will normally be recoverable by quarterly deductions from the remuneration payable by executive councils to individual members of the group. Great flexibility is shown in the conditions laid down for these loans. Thus, it has been decided not to prescribe a standard term of years for them. Although it is suggested that the normal period should be 10 years and should not in any case exceed 20 years, the period of repayment "should depend as far as possible on the circumstances of a particular application." Application for a loan may be made by general practitioners taking part in general medical service who propose to form a group practice or who, having formed a group, propose to provide new practice premises or substantially to improve the existing premises. Assistance by means of these loans will be available for the following purposes: (*a*) the erection of a new building, either on land already owned by one or more of the members or on land which may have to be acquired for the purpose and for the acquisition of such land; (*b*) the acquisition of an existing building and its conversion into surgery premises; and (*c*) the conversion of a building already owned by a member of the group.

Combined Diphtheria Toxoid and Pertussis Vaccine and Poliomyelitis.—A correspondent in the *British Medical Journal* (**1**:215, 1954), draws attention to the possible clinical implications of some experimental work carried out by Anne McLaren in the department of zoology and comparative anatomy, Oxford. Mice infected with the virus of mouse encephalomyelitis (GDVII strain) were given injections of alum-precipitated diphtheria toxoid and a pertussis vaccine 48 hours after the injection of the virus. The diphtheria toxoid had been prepared in October, 1950, and was marked as fit for use until October, 1952. The date of manufacture of the pertussis vaccine was not known. When first tested in February, 1951, the combined toxoid and vaccine increased about tenfold the susceptibility of mice to virus given 48 hours previously, but a month later treatment with the same batch of immunizing agents produced little or no apparent increase in susceptibility and in September they decreased nearly tenfold the susceptibility of the mice to virus. This protective action was confirmed by further experiments in November and December. The probability of the apparent protective effect observed in these experiments arising as a result of chance variation alone is said to be less than one in a thousand. The series of experiments was repeated with fresh immunizing agents in 1952 with the same results. The effect did not appear to be related to the season of the year, and it is therefore concluded that the properties of one or both of these agents were altering with age. No explanation of the protective effect of the aged toxoid and vaccine is offered at this stage. It does not necessarily follow that giving a child injections of diphtheria toxoid will protect him against poliomyelitis, but the principle brought to light by McLaren, that the influence of certain immunizing agents on an animal's susceptibility to a neurotropic virus depends on the age of the inoculum, may possibly be a fundamental one. If so, it is important to ascertain if that principle has a clinical application.

Infantile Gastroenteritis.—The striking fall in the death rate from diarrhea and enteritis among London children under the age of 2 years is discussed by Ian Taylor (*Lancet* **2**:202, 1954). Deaths per 1,000 live births have fallen from 23.8 for 1891 to 1895 to 0.8 in 1951. Expressed as a percentage of the 1931 to 1935 rate, which was 11.6, this gives a range from 205 for 1891 to 1895 to 7 in 1951. In an attempt to explain this dramatic fall, attention is drawn to certain factors. For instance, the rate of improvement has been greater in London than in the rest of the country. Improved treatment, better social conditions, and health education have undoubtedly all played a part in producing this amelioration, but other factors must be considered. Thus, a recent survey of admissions for gastroenteritis showed that about one in five of the patients were regarded as being ill enough to justify parenteral therapy. Before World War II the case-fatality rate in the London hospitals was about 20% of admissions. "Unless it is assumed that all the infants at present receiving intravenous therapy would have died without this treatment, one is led to the conclusion that the proportion of severely ill patients admitted to hospital is smaller than in pre-war years." Then again, in the London boroughs in which gastroenteritis must be reported, the fall in incidence did not occur until 1946, when the death rate had already been falling for three years. Finally, the severe epidemic form of gastroenteritis in nurseries has been less common in recent years. "The fact that the prevalent mild form of dysentery spreads easily in nurseries suggests that the rarity of gastroenteritis epidemics is due to reduced prevalence of the causative micro-organism rather than to improvements in hygiene. . . . Whether this reduction in incidence has come to stay remains uncertain."

Fatal Bronchial Asthma.—A series of 18 fatal cases of bronchial asthma was reviewed by C. Kelman Robertson and K. Sinclair in the *British Medical Journal* (**1**:187, 1954). They were all patients in the Royal Infirmary, Edinburgh, between 1939 and 1952, and their ages ranged from 14 to 67 (only one was under 41 and only three were over 59). Necropsy was performed in each case. Eleven of the deaths occurred in the months of September and October. Two modes of death were apparent: sudden and unexpected in 13 and progressive exhaustion with terminal coma in 5. The duration of the fatal attack varied from a few minutes to 12 days. At necropsy, all patients had mucous plugs in the bronchi and all but one had eosinophilia. The right ventricle was hypertrophied in seven. It was recommended that a patient in an acute attack who shows signs of increasing dyspnea and cyanosis within a few hours, in spite of attempted control, be hospitalized immediately. If there is no cardiovascular contraindication, an immediate injection of 1.2 ml. of a 1:1,000 solution of epinephrine hydrochloride should be given; if this is contraindicated, 0.25 gm. of aminophylline is given intravenously. The early use of a mixture of 95% oxygen and 5% carbon dioxide at a rate of 6 liters per minute is recommended. Safe sedation is produced by 0.2 gm. of phenobarbital sodium given intramuscularly. For rendering the sputum less viscid, 0.6 ml. of potassium iodide in the form of strong iodine (Lugol's) solution given thrice daily is recommended. In the presence of respiratory infection, penicillin should also be given. If all this fails, cortisone or corticotropin (ACTH) may be given, the risk of fluid retention leading to heart failure being borne in mind.

Bureaucratic Bumbledom.—Blackburn is a Lancashire cotton town with a population of 111,000, served by 71 general practitioners, 66 of whom are on the obstetric list. It has one general-practitioner maternity home with 20 beds, the Springfield Maternity Home. Last December, without any consultation with the official local body responsible for organizing the general medical service or with the local branch of the British Medical Association, the Blackburn group hospital management committee and the Manchester regional hospital board announced that this home was to be closed as a maternity center on the grounds of redundancy and to be reopened as a geriatric center. A strong protest was registered by the local council, and an appeal was made for no action to be taken until the matter had been further discussed by the council. This was ineffective, and on Jan. 8 the home was closed. According to a report in the supplement to the *British Medical Journal*

(1:22, 1954), "It is understood that the doctors concerned were not notified of the date of closure and that the patients themselves had barely 24 hours' warning." "But," in the words of an editorial in the same issue, "most disturbing of all is the report that the evacuation of the Springfield Home was carried out on the orders of a lay official at short notice and without any opportunity for the doctors concerned to decide upon the fitness or otherwise of their patients to be moved. If this is true it represents an interference with a doctor's clinical responsibility which is quite beyond the right of any administrative authority."

B. M. A. and the World Health Organization.—The published proceedings of a recent meeting of the council of the British Medical Association states: "A letter with some well-known signatories was read proposing a 'United Kingdom Committee for the World Health Organization of the United Nations.' This would be a specialized body to study closely the work and plans of W.H.O., organizing meetings and giving assistance to the Organization in a number of ways which were set out. The chairman of council said that he thought inquiries should be made of the sponsors of the new organization as to any ways in which the B.M.A. could be of service, but, of course, the interests of the B.M.A. in W.H.O. were in charge of the World Medical Association."

Driving Licenses.—A memorandum approved by the council of the British Medical Association for transmission to the Ministry of Transport contains a recommendation that, when a driving license has been suspended, the court before its restoration is approved shall have power to require a medical certificate to the effect that the applicant is medically fit to drive, and that such a certificate shall normally be required as a routine.

SWEDEN

Statistics of Legally Induced Abortions.—The abortion law of 1939, with its supplement in 1946, has been put into effect with such great and growing frequency that it has created problems of major importance. A critical and statistical analysis by Dr. Klintskog in *Nordisk medicin* for Jan. 2, 1944, of the 27,000 legal abortions induced in the 12 year period 1939 to 1950 shows how some of the original calculations concerning the outcome of this legislation have been falsified by events. For example, it had been expected in some quarters that with the rapid advances now being made in therapeutics and preventive medicine, the number of patients with strictly medical indications for the legal induction of abortion would show a satisfying decline. The experience of these 12 years, however, shows a steadily rising abortion rate for most of the ailments for which legal abortion is granted. Even pulmonary tuberculosis, with its rapidly declining mortality, is no exception in this respect. In 1940 pulmonary tuberculosis was the indication for the induction of abortion in 131 cases. The corresponding figure for 1950 was 290. The abortions induced for heart disease rose from 27 in 1940 to 70 in 1950. In 1940 the toxemias of pregnancy, nephritis, and hypertonia were the indications for 30 abortions and in 1950 for 90. Organic disease of the central nervous system was represented by only 6 cases in 1940 as compared with 55 in 1950. Diseases of the internal secretions had about the same effect, with only 6 cases in 1940 as compared with 47 in 1950. Among diseases of the blood, anemia was not represented by a single case in 1940 and by only 3 in 1941, but in 1950 there were 10 such cases. Dr. Klintskog could not definitely account for these findings, but he suggested that (1) several patients at the beginning of the period under review might have been suitable candidates for abortion, which was not induced because the indications were overlooked; (2) facilities for the diagnosis of diseases qualifying for abortion might have been increased of late; (3) physicians might have changed their attitude toward certain diseases supposed to qualify for abortion; (4) changing social conditions, such as housing problems, might have influenced physicians' opinions; and (5) the public, as well as the medical profession, might have modified its views on the subject.

Prevention of Iatrogenic Disease.—Of late, geriatric problems, psychosomatic disease, and iatrogenic disease have been popular in the Scandinavian medical press. Dr. Forssman, a psychiatrist, has recently analyzed in *Nordisk medicin* the characteristic features not only of the patients most likely to have iatrogenic disease but also of the physicians most likely to inflict it on their patients. The hypochondriac succumbs most readily, but patients with poor mental development also misinterpret physicians' spoken and written words. The physician who creates iatrogenic neuroses is apt to be of the anxious, overconscientious type, not sure of himself and inclined to hedge. He dislikes taking responsibility for a categorical reassurance of his patient and may prescribe "just a little digitalis for safety's sake." Admitting that he has not found anything definitely wrong with the heart, he adds: "But be a bit careful on walking upstairs." Having admitted the existence of several cheering phenomena, he tempers their cumulative effect with the reservation: "Of course we can't be 100 per cent sure of ourselves." Dr. Forssman finds that iatrogenic neuroses are most likely to develop as the outcome of radiological and electrocardiographic examinations and the measurement of the blood pressure. Not only the variety of these tests but also the variety and number of physicians the patient meets help to promote iatrogenic disease, which is much less likely to be fostered when the family doctor is the sole medical expert the patient is required to meet. The many physicians who have examined the patient send reports in writing about her to each other, and, when she gets a glimpse at such reports and misinterpets them, she may be badly shocked as in the case of the woman who read a memorandum on her case in which she was said to be suffering from cancerophobia. She did not know what phobia meant, so she jumped to the conclusion, already dormant in her mind, that she was suffering from cancer. In their reports to each other, physicians would be well advised to write what it is they have said to a patient so that misquotation may be reduced to a minimum. They should also not let patients overhear what is said to medical students, nurses, and others concerning diagnoses and prognoses. Above all, they should distinguish between persons likely and not likely to have iatrogenic disease.

The Late Professor Schaumann and Benign Lymphogranulomatosis.—The death from coronary thrombosis on Aug. 9, 1953, of Prof. Jörgen Schaumann has drawn attention to his most important life's work, the identification of benign lymphogranulomatosis. He was born in Sweden on June 3, 1879, and, though he figured prominently at international meetings of dermatologists, most of his work was done in Sweden, where he had been professor of dermatology since 1939. Only five days before his sudden death he was correcting the proofs of his last original article, which has now been published in the *Annales de dermatologie et de syphilographie*. His pursuit of the solution to the problems of lupus pernio, sarcoidosis, and allied conditions lasted the better part of a lifetime. As early as 1914, he concluded that Boeck's sarcoid and lupus pernio are genetically identical, representing a disease of the lymphatic system and coming under the comprehensive title of benign lymphogranulomatosis. Behind its cutaneous manifestations he found more deep-seated localizations of this disease in the lymphatic glands, tonsils, bone marrow, spleen, liver, and lungs. Lupus pernio and the cutaneous sarcoids, he believed, should be regarded as inconstant and accessory localizations in the skin of this general disease. In other words, it might exist without any skin manifestations whatever. In 1935 Schaumann reported to the British Association of Dermatology and Syphilis on four patients with this disease examined at post mortem. He pointed out that the commonest cause of death in such cases was ordinary tuberculosis. As late as 1946 he gave an account of studies he had undertaken with Dr. G. Seeberg with regard to tuberculin tests. His suspicion that benign lymphogranulomatosis is a manifestation of tuberculosis was tempered by his sense of the complexity of this problem.

CORRESPONDENCE

FACTS REGARDING OLDER PERSONS

To the Editor:—Readers of THE JOURNAL may be interested in some of the data recently made available by the United States Census Bureau concerning our older population. It was estimated from the 1950 census that, of a total population of 150,700,000 persons of all ages in the continental United States, 12,270,000 (8.1%) were 65 years of age and over. Included are 3,850,000 persons 75 years or older, of whom 4,475 were reported to be 100 years of age or older.

A relatively small number of our older persons were living in institutions at the time of the interview, since only 3.14% of all who were 65 years and over were estimated to be in homes for the aged, nursing homes, chronic disease hospitals, mental hospitals, tuberculosis hospitals, correctional institutions, and institutions for the mentally handicapped. Although the rate of institutionalization increased progressively with age, only 9.41% of those who were 85 years of age and over were in the various institutions. Thus, almost all of the older persons in the United States were living outside of institutions, and, even among those who were 85 years and older, slightly more than 90% were living independently or with their family or friends.

In addition to the census reports, data regarding the average remaining life expectancy of older persons in the United States are also worthy of note. The estimate for 1950 made by the National Office of Vital Statistics, U. S. Public Health Service, was 14.1 years at age 65, 11.2 years at age 70, and 8.7 years at age 75. One of the several conclusions that may be drawn from this is that roughly half of those persons who were 65 years of age would live to, or exceed, the expected 14.1 years. Some will live 20 or 30 and a few even 40 more years after reaching their 65th birthday. Since there is no way to determine ahead of time what a particular person's life span will be, those who are 65 years of age should plan their affairs around the possibility of living for a longer period. The realization of these facts should be useful to persons who retire at age 65 for reasons other than disability and illness, as well as to their advisors, and should serve to encourage older men and women to seek a useful, active life for their remaining years.

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SALT-POOR DIET AND JEWISH DIETARY LAWS

To the Editor:—Dr. Bruno Kisch's letter dealing with salt-poor diet and Jewish dietary laws (THE JOURNAL, Dec. 19, 1953, page 1472) was read with both professional and personal interest. It is very important for the physician to obtain the full cooperation of his patient. If the patient happens to be a person who adheres strictly to the Jewish dietary laws, the physician should be able to advise him to prepare a diet that will enable him to stay within his religious precepts.

According to Dr. Kisch's experiments, a religious Jew on a salt-restricted diet should "cook the meat in a generous amount of fluid, and throw the broth away." This calls forth several observations. Dr. Kisch's experiments were made with meat that had been salted for the customary one hour. However, the coded law in "Yoreh Deah," chapter 69, paragraph 6, states that the meat should stay salted for precisely 18 minutes, but the custom is to let the salted meat stand for a complete hour. The law also states that on arrival of unexpected visitors for whom meat has to be prepared in haste or when the imminence of the Sabbath infringes on the cooking time, it is permissible to let the meat stand for only 18 minutes. In the case of a sick patient for whom a salt-poor diet is essential in treatment and may even prevent catastrophe, the meat certainly would be allowed to remain salted for only 18 minutes. This is especially so since the Jewish religion elevates to a law the striving for and maintenance of good health.

Dr. Kisch expressed the opinion that "salted" meat should be eaten only boiled and not fried or broiled. In regard to frying meat in a pan, I am in full agreement with Dr. Kisch. Obviously, this situation allows the meat to come in contact with the dripping blood. The question of broiling is another matter entirely. In this instance I cannot agree with Dr. Kisch. According to the Jewish law, roasting meat directly over glowing coal, charcoal, or above flame does not require the preceding salting process. Broiling of meat (where the heat strikes from above) is considered by the majority of orthodox rabbis as roasting (*Hapardes,* November, 1951). There is a custom to salt the meat destined to be roasted, but in the event of sickness this practice certainly could be omitted. Moreover the custom of salting meat to be roasted cannot be compared with the salting of meat to be boiled. The salting process as applied to roasted meat is very sparingly employed. There is no need to allow the salt to stand on the meat for any length of time. Just the act of "salting" is needed as a customary procedure, the salt then could be rinsed off immediately.

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PROGESTERONE AND CARCINOMA OF THE CERVIX

To the Editor:—We have previously reported some observations on the effect of progesterone on carcinoma of the cervix. These require reconsideration in the light of additional experience. We have described certain superficial alterations in the clinical appearance of cervical carcinomas in patients receiving progesterone that led us to conclude "that cervical carcinoma can be substantially altered by steroid hormone administration." We stated: "In some instances those changes have been somewhat comparable to the hormone-induced regressions seen in breast carcinoma under estrogen therapy." Subsequent experience under more appropriately controlled clinical conditions leads us to conclude that progesterone administration, under the time and dosage schedules we have employed, has no material effect on cervical cancer or on the clinical manifestations of the disease.

In retrospect, it appears that our initial erroneous conclusions probably arose from (*a*) too great reliance on serial photographs, without proper allowance for the varying visual effects that can be obtained by slight alterations in perspective or by manipulation in preparing the field for photography and (*b*) our lack of appreciation of the spontaneous variability in the gross clinical appearance of malignant lesions of the cervix and too great dependence on clinical appraisal of such lesions by means of visual inspection and palpation. We had previously reported that: "Routine histopathological study of the biopsy and surgical specimens has not indicated the morphological basis for the observed changes" (*J. Nat. Cancer. Inst.* **11**:867, 1951). Further study of these materials indicates no morphological deviations from the usual abnormalities encountered in comparable cases of cancer of the cervix.

Although some readers apparently interpreted our report as a therapeutic claim, our actual statements in this regard were as follows: "We do not consider the regressive changes observed to be sufficient to indicate the use of progesterone as a therapeutic agent in carcinoma of the cervix" ("Symposium on Steroids in Experimental and Clinical Practice," New York, Blakiston Company, 1951). And we also said, "Irrespective of the regressive changes, we do not consider progesterone to have added anything materially from the clinical standpoint to the therapy of cervical carcinoma" ("Proceedings of the Second Conference on Steroids and Cancer, Committee on Research of the American Medical Association, April, 1951, p. 113).

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EXPERIMENTALLY INDUCED CONGENITAL DEFECTS IN MAMMALS

To the Editor:—In the past few years there has been mounting interest in the experimental production of congenital malformations in mammals and in attempts to apply the results to humans. This interest stems partly from the fact that advances in the treatment of bacterial infections now make it inevitable that many infants with severe deformities, who would formerly have died soon after birth, will now live for long periods. Those with less obvious abnormalities may survive a lifetime as medical problems and social liabilities. It is, therefore, important to view critically the relation of mammalian experiments to abnormal human development.

Human congenital abnormalities—anatomic, physiological, and biochemical defects present from the time of birth—are often divided by those interested in preventive medicine into two groups, genetic and acquired. A genetic defect is due to a fault in the make-up of the sperm or the egg, probably in the genes. An acquired defect results from injury to the embryo or fetus during development by some environmental agent. Although the genetic constitution of a person determines whether or not he will be susceptible to a given environmental agent, we arbitrarily separate environmental from genetic influences in practice. Genetic faults, which may be passed on from generation to generation, can operate in many complex ways. Hemophilia is an example of biochemical or physiological congenital abnormality caused by a faulty gene that usually shows itself soon after birth as a defective development of the bodily chemistry that governs the blood clotting mechanism. Thomsen's disease, a congenital myotonia, is another genetic example of a physiological or biochemical disorder in which the mechanisms for muscular contraction and relaxation mature abnormally. Deformities of the fingers or skeleton, such as syndactyly and chondrodystrophic dwarfism, illustrate anatomic malformations that are present from birth and that have their origin in abnormal genes. Some genetic defects, especially anatomic ones, are indistinguishable from those acquired during development. This is because a specific interruption of the development of a part of an embryo at a certain stage leads to a specific deformity; whether a faulty gene makes the embryonal part go wrong at this time or some environmental factor acts on it may make no difference in the outcome. In isolated cases of human congenital defects, therefore, it is often very hard to know which factor is to blame. Only when a large family and several generations happen to be available for study —a rarity in human biological studies—can the genetic origin be reasonably established.

Acquired defects can have their beginnings at any time during development. Although one usually thinks of these as being at the anatomic level, there is certainly no reason to believe that abnormalities at the biochemical or physiological levels cannot be acquired. Acquired defects can result from chemical, physical, infectious, or traumatic agents, but in human beings the agent is seldom known. Rubella (German measles) and ionizing radiations in therapeutic dosage are examples of environmental agents that may cause human congenital abnormalities by acting on certain vulnerable parts of the embryo at specific times during gestation. This radiation effect, of course, differs from its genetic effect, demonstrated in mammals and presumed possible in man. Many other agents, such as bacterial and viral infections, metabolic and nutritional disorders, endocrine conditions, and a wide variety of drugs, have been suspect, but in any given case the relationship between the congenital abnormality and the supposed agent is difficult to prove. Anoxic, infectious, or mechanical injuries at birth may be responsible for interruption of developmental processes still active at that time and may lead to subsequent defects. It is also important to remember that acquired congenital abnormalities are not only the result of interference with embryonal tissues but also the result of destruction of structures that have already attained a fairly mature state. The physician who, confronted by an anatomic malformation, tries to reconstruct the pathological process that brought it about quickly realizes that the total infant is a result of a sequence of complex interlocking developmental systems that mature at different rates, and a solution of the puzzle may be impossible.

Experimental work in the field of abnormal mammalian development has concentrated particularly on the etiological role and to a lesser extent on the mechanisms of action, of various noxious agents in the production of developmental defects. For the most part, the defects have been primarily anatomic, since they are the easiest to recognize. A great many agents and procedures have been employed, mostly with the aim of determining that defects do result and less often to learn the precise mechanisms and time factors involved. All sorts of patterns of deformity have been produced ranging from severe abnormalities of the nervous system and skeleton to visceral and vascular anomalies. The work with which I have been connected seems to indicate that three factors determine what form the defects will take—the time at which the agent injures the embryo, the nature of the agent that determines what tissue it will attack, and the capacity of the developing tissue to repair itself.

What stands out in most investigations is that the doses used in the case of chemicals, drugs, etc. are relatively enormous and translated into human terms would amount to gross poisonings or massive overdoses. At best they usually imitate circumstances in which the pregnant woman would almost never be found. Vitamin A, nitrogen mustard, and some other anticancer agents, several steroids, prolonged anoxia, and some dyes are among those agents that have been shown to cause embryonic or fetal injury with resultant abnormal development.

In our own laboratory, we have examined the pathological effects of more than 50 agents on pregnant or newborn rats and mice with a primary view to learning something about the metabolism of developing tissues that makes them biochemically vulnerable to one agent and resistant to another. Several steroids, including cortisone and testosterone given to newborn rats and mice, cause severe necrosis of developing cells in the brain, general stunting of growth, abnormal skeletal growth, destruction or impaired development of hair follicle cells, and certain other organ changes. Some of these pathological alterations occur in fetuses if the pregnant animal is given the drug. The dose necessary to produce these effects is enormous. Cortisone in 0.25 to 1 mg. doses to a 1 gm. infant mouse amounts to 250 to 1,000 mg. per kilogram. Assuming no species difference in susceptibility between man and mouse, it would require somewhere between 2 and 10 gm. of cortisone to elicit a comparable effect on a 10 kg. human infant. When the dose in a baby mouse is reduced to 0.01 mg., there is no appreciable deleterious effect; indeed the massive dose is sometimes not very effective experimentally unless repeated. Similarly, if aminopterin, nitrogen mustard, triethylene melamine, or triethylene phosphoramide, which mimic some of the effects of radiation on mammalian embryos, were to be literally translated from animal to human doses, it would require enormous amounts of the drugs, far in excess of that used therapeutically, to damage the embryo or fetus seriously. Again when the massive dose in animals is scaled down 5 to 10 times, it may have no measurable effect on development, yet even this reduced dose is many times, proportionately, what would be used in cancer therapy in man.

The same quantitative problem seems to apply to the recent experiments of Cohlan who administered daily doses of 35,000 units of vitamin A to pregnant rats and thereby produced congenital malformations. Carried over to humans, this would be more than 5,000,000 units daily. Similarly, we have had to give relatively large, repeated doses of propylthiouracil to newborn or pregnant animals to induce histological developmental changes; otherwise, no measurable abnormalities resulted.

These examples are not given to discredit in any sense the value of such experiments to the science of mammalian embryology and abnormal development or to relegate them to the category of "laboratory stunts." Indeed they have taught us much about how malformations may come about. Rather, my point is to urge the use of common sense in interpreting animal experiments and point some directions in which new research may go. There are already some mammalian experiments in progress that come closer to imitating human circumstances than most; for example, the dietary experiments of Warkany and Wilson and their associates at the Cincinnati Medical

School, Children's Hospital, in which a variety of malformations have resulted from deficiencies in the diets of several vitamins. Such experimental conditions might closely approach the human dietary conditions now present in some parts of the world. In our own, as well as in other laboratories, some related deficiency experiments are in progress as well as the more artificial type of experiment in which antimetabolites of dietary constituents are used.

All in all it would seem that much progress in congenital malformations could be made in three directions. 1. Current empirical experiments on drugs, chemicals, viruses, and other noxious agents that may harm embryos might be extended, for these form the groundwork for determining what might affect humans. 2. More experiments that closely simulate human circumstances might be encouraged. Such procedures can be screened in small laboratory animals where large numbers of observations are essential and then possibly carried over to primates. 3. The results of animal experiments might be compared critically with data now being gathered in many clinics on the genetic, environmental, and gestational backgrounds of mothers who have abnormal children.

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NOCTURNAL ENURESIS

To the Editor:—I should like to comment on the editorial "Nocturnal Enuresis" that appeared in the Feb. 6, 1954, issue of THE JOURNAL, page 509. Considering the wide incidence "involving about 16% of the population between the ages of 3 to 15 years" and that 97% of those affected have no "anatomic or physiological abnormalities," it seems remiss that personality factors are not referred to more fully in the editorial. The persistence of the symptom into adulthood was also strikingly shown among Selective Service draftees. The search for hereditary explanations, organic cerebral causes, simple medicaments, and conditioned reflex treatments cannot take the place of adequate personality evaluation in finding the roots of this maldevelopment. In the majority of cases, nocturnal enuresis is due to a lack of self-control caused by a fault in the child's upbringing, a chronic anxiety state, or an early psychoneurosis. The defect is in the child, not in the urinary system.

Nocturnal enuresis is only a symptom. Symptomatic treatment is as illogical here as would be the mere removal of the cough in pulmonary tuberculosis or the use of morphine to remove pain in appendicitis. Many other personality symptoms are associated with nocturnal enuresis including anxiety, behavior disorders, and fears. The enuresis may be the result of inadequate training from the beginning of infancy (rejection or overprotection by immature, psychoneurotic, or anxious parents) or regression from a well-established sphincteric habit caused by a psychic trauma (birth of a sibling, death of or separation from a parent, or a physical illness). It is not the symptom of enuresis that is significant but the total personality maldevelopment; this may lead to persistent personality distortions (immaturity, delinquency, and antisocial behavior); or it may lay the ground for other psychopathological complications.

We should certainly recognize valuable studies of different aspects of a symptom and collate these periodically. However, is it not more important to reemphasize total diagnostic and etiological, rather than symptomatic, approaches for good treatment?

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USE OF FOAM RUBBER

To the Editor:—The article by Dr. Maurice Gershman in the Jan. 23, 1954, issue of THE JOURNAL suggested that foam rubber should be more scientifically defined as a matrix of latex rubber fibers through which runs a continuous maze of air channels that gives the structure a porous nature. Dr. Gershman's definition of foam rubber as an infinite number of air bubbles in a matrix of rubber is technically a description of sponge rubber, which is not porous. In certain processes of gluing foam rubber to itself or to a cloth backing, the porous structure is sealed off. More recently a process of applying the cloth directly to the foam retains porosity of the rubber, and the rubber can be used as Dr. Gershman suggested without perforation when applied directly to the skin. The foam rubber material must, however, be free of irritating chemicals and of foreign matter and must be of light weight.

During the past two years my interest has been directed to the increasing use of foam rubber products by the medical profession. Since the foam rubber industry is centered in Ohio, this afforded me the opportunity to study its modes of manufacture and its physical and chemical properties. I was supplied by numerous companies with quantities of their products for use as bandages. It is now very evident by the many articles being published as to the uses of foam rubber in medicine that my interest in this material was not an idle one. The many other uses found for supported foam rubber of good quality are padding under casts, elastic roller bandages, especially where complete milking of an extremity is desired before surgery, splinting the chest wall, and many other circular bandages. The foam rubber supported by elastic cloth as well as that with fixed cloth backings should soon be more available. If purchased from medical supply houses it should be a quality that will be safe to use directly on the skin or even to apply over an open wound.

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SOCIALIZED MEDICINE

To the Editor:—After obtaining his medical degree in England, Dr. P., to escape socialized medicine, came to the United States where he worked in hospitals in order to secure training in a specialty. Meanwhile his wife worked as a laboratory technician in the offices of various physicians, thus having the opportunity to see first hand and from the inside what we may fairly consider the highest type of the practice of medicine. For more than a year, she was in the office of four physicians, each of whom is on the faculty of a medical school, two with professorial rank. Last summer Dr. and Mrs. P. visited for a few months with their families in England. A quotation from one of her letters is very revealing.

"I cannot tell you how disgusted we are with socialized medicine. It seems to me both patients and doctors are suffering. Doctors are limited in the number of antibiotics and drugs they can prescribe per year, and if they exceed their quota they can be heavily fined or struck off the register. Patients are not receiving adequate care, and doctors are not able to give it. Two examples of this are in my own family. My father-in-law is quite a sick man being partially crippled with osteoarthritis of the spine, an old coronary patient, and a very chronic diabetic who has an insulin reaction almost every day. He has not had a blood sugar determination done for eight years, and the only urinalysis he has had has been the Clinitest he does himself. The other example is my mother who has had some bleeding and who has frequent dizzy spells. I persuaded her to see a specialist on Harley Street as I thought she might be anaemic. The specialist took her blood pressure, listened to her chest, charged her $15, and told her she was not anaemic. Not even a blood cell count! Once a patient is entered into hospital his own doctor cannot follow him through, and for any lab, x-ray, electrocardiogram studies, the patient must get a letter from his practitioner, go to the outpatient department at the hospital, be re-examined by the resident, and then gets his lab work done. We hope socialized medicine never comes to the United States."

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RHEUMATIC AND FEBRILE SYNDROME

To the Editor:—I was most interested in the article on a rheumatic and febrile syndrome during hydralazine treatment by Dunstan and her colleagues (*J. A. M. A.* **154:**23 [Jan. 2] 1954). Last June I reported (*Ann. Rheumat. Dis.* **12:**98, 1953) a similar syndrome that appeared spontaneously in middle-aged and elderly patients. It was characterized by prolonged fever, diffuse aching of muscles and joints, a high blood sedimentation rate, and changes in the plasma proteins similar to those found by your contributors. Other features included diarrhea, vomiting, conjunctivitis, erythematous rashes, splenomegaly, lymph node enlargement, anemia, leukopenia, and chest signs. Recently, a similar syndrome has been seen in young persons with more acute manifestations. In no case was there pleural effusion or ascites. This will be described in a future paper.

The disease appears to be more closely related to rheumatoid arthritis than to the other connective tissue diseases, and I have suggested the name anarthritic rheumatoid disease for those cases in which the joints are not involved. In the young, the disease is severer and may resemble acute disseminated lupus erythematosus. Intermediate forms occur resembling true rheumatoid arthritis. In 10 cases the prognosis was excellent, and there were no sequelae. The disease may, however, last for months or years with remissions.

The syndrome developing after hydralazine therapy appears to be closely related to the disease described above and emphasizes the overlapping nature of connective tissue diseases in general. As the authors suggest, the syndrome appears to be no ordinary drug hypersensitivity, but some alteration in tissue metabolism as found in rheumatoid disease or acute disseminated lupus erythematosus. Does hydralazine act as an inhibitor of some cortical hormone that normally prevents the rheumatic state from developing, or can it act by causing adrenal cortical exhaustion in some cases? The stress of hypertension and of prolonged drug administration may have been the trigger mechanism. Three of the seven patients reported on in my paper had undergone an exacting experience, such as operation, immediately before the symptoms developed. It is interesting that a similar clinical picture may arise spontaneously and after hydralazine therapy.

The presentation of these atypical connective tissue syndromes helps us to realize the link that may exist between all of them. The clue to the pathological process may well be found in their study.

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USE OF THE METRIC SYSTEM

To the Editor:—The article in The Journal (**154:**263 [Jan. 16] 1954) with this same title fails to mention that what is called the "divorce" of the unit of volume, the liter, from the unit of length, the meter, is in reality negligible for nearly all practical purposes; 1 liter = 1.000027 $dm.^3$ (Pharmacopoeia Helvetica, p. 2). Therefore 1 ml = 1.000027 $cm.^3$; 1 microliter = 1.000027 $mm.^3$ In Great Britain, where, unfortunately, the metric system is used too little, "mils" are mostly used in scientific publications, whereas on the European continent it is legal to use $cm.^3$ instead of milliliter in all cases where the precision asked for is less than 1/10,000th.

In this connection it might be mentioned that most readers who do not speak English would be very pleased, if all scientific publications in English would use either the metric system only or give the equivalents in the metric system. Also it would be appreciated if animals and plants were mentioned not only by their English name but also by their international (Latin) designation. If these two points were observed generally, most scientists in countries where English is not generally spoken would probably look at English as the most suitable international scientific language.

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COUNCIL ON MEDICAL SERVICE

A. M. A. POLICY ON VETERANS' MEDICAL CARE

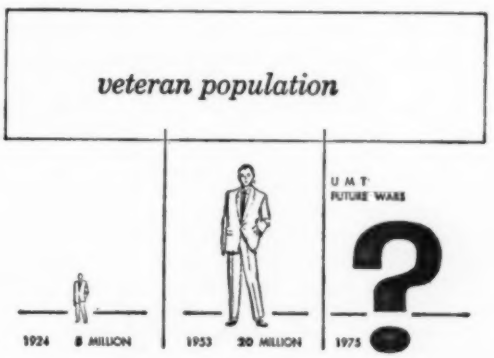
This is the third in a series of articles prepared by the Committee on Federal Medical Services of the Council on Medical Service to explain the A. M. A. position on medical care for veterans with non-service-connected disabilities and to provide background information on the subject. The second article appeared in The Journal, *Jan. 30, 1954, page 441.*

Louis M. Orr, M.D., *Chairman,*
Committee on Federal Medical Services.

Our Veteran Population

It has been pointed out frequently that the United States rapidly is becoming "a nation of veterans." That fact alone calls for serious reconsideration of our national policy regarding tax-paid hospital and medical care provided by the federal government through the Veterans Administration. The basic legislation governing the current VA medical program was enacted 20 years ago when our veteran population was only a fraction of its present size. That legislation, applied now and in the future to a much larger, continually growing and steadily aging veteran population, creates medical, economic, and social problems of vital concern to all citizens. After careful consideration of those problems, the House of Delegates of the American Medical Association in June, 1953, took a position that can be summarized as follows:

1. Veterans with diseases or disabilities caused or aggravated by their military service are entitled to the best possible hospital and medical care from the Veterans Administration.



The U. S. veteran population now includes about 40% of all adult males. Under existing legislation, the federal government is obliged to provide "free" medical care for many of these veterans, if they request it. The medical profession questions the soundness of providing medical care at federal expense to veterans with non-service-connected disabilities. It is likely that by 1975 the U. S. will truly be a "nation of veterans." If the VA medical program continues to accept responsibility for the care of veterans with service-connected and non-service-connected disabilities alike it is difficult to see how a complete federal health program can be avoided.

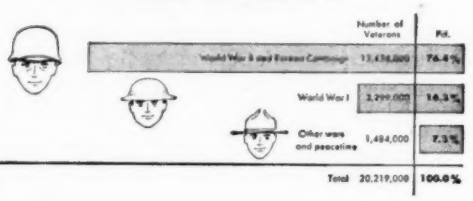
2. War veterans with tuberculosis or neuropsychiatric disorders of non-service-connected origin, who are unable to pay for their own care, should continue to receive VA hospital and medical care, within the limits of existing facilities, until such time as local facilities are adequate to take care of them.

3. VA hospital care for all other veterans with non-service-connected disabilities should be discontinued, and the responsibility for their care should revert to the veterans themselves, or, if they are indigent, to their communities.

New legislation limiting the scope of the VA medical program has become necessary because, as a result of World War II and the Korean combat, we now have more than 20 million veterans in this country. Our veteran population has been increasing steadily during recent years, and it will continue to increase at an unpredictable rate in the immediate future. In the event of another major war, of course, there again would be a large rise in the number of veterans.

analysis of veteran population

PERIOD OF SERVICE



Taxpayers should note that as veterans grow older they require more frequent and increasingly longer periods of hospitalization. World War I patients are now hospitalized twice as long, on the average, as World War II patients with similar disabilities. World War II veterans, relatively young and comprising 76% of the total veteran population, present a costly long term responsibility to U. S. taxpayers. The medical profession recommends medical care through the VA for only those veterans with service-incurred disabilities and temporarily for those with tuberculosis or neuropsychiatric conditions of non-service-connected origin.

AGE DISTRIBUTION (Exclusive of those discharged on or after June 27, 1950)

DATE	JAN. 1, 1952	JAN. 1, 1960	JAN. 1, 1970
TOTAL	18,850,000	18,160,000	16,146,000
AGE 22-44	77.2%	62.7%	13.5%
45-64	21.8%	27.4%	73.7%
OVER 65	1.0%	9.9%	12.8%

Older veterans are hospitalized more frequently for civilian-incurred ailments than for service-connected disabilities. By 1970, over 86% of the present veterans will be age 45 or over, more than three times the number in this older age group today. Because of advanced age, they will require more frequent and prolonged hospitalization for illnesses having no relationship to their military service. Responsibility for such medical care should be assumed by the individual or local government, not by the federal government.

The size of our veteran population is not the only factor pointing to a tremendous future expansion of the already vast VA medical program. Of equal importance is the age of our veterans, for as they grow older they naturally will be subject to a greater number and variety of ailments, especially those of a chronic nature. With some 20 million veterans permitted to turn to the federal government whenever they believe or claim that they cannot pay for their own hospital and medical care, continuation of the present VA policy in the years ahead will have a major influence on clinical problems, length of hospital stay, costs, personnel requirements, and the amount and types of facilities necessary. Past experience of the Veterans Administration shows that, as the postwar years pass, the number of service-connected cases declines, that of non-service-connected cases rises, and the average length of hospital stay increases.

With these facts in mind, a comparison of the present and future composition of our veteran population will help to illustrate the magnitude of the problems looming ahead. Our veteran population today is composed mainly of two large groups, which together account for about 90% of the total—the World War II veterans, mostly under age 40, and the World War I veterans, predominantly over age 50. As of Dec. 31, 1953, when there were 20,458,000 veterans in civilian life, more than 75% were World War II and Korean war veterans and more than 16% were veterans of World War I. At the beginning of 1952, the average age of the World War II veterans was 32.8 years, and the average age of the World War I group was 58.2 years. Among the smaller groups of veterans, those of the Spanish-American War averaged 75.2 years of age, while those with service only since the start of the Korean campaign had an average age of 22.1 years.

Looking ahead only 16 years to 1970, and not including peacetime veterans, Korean veterans, or any future addition to the veteran population, an estimated 16,146,000 of our present veterans will still be alive, practically all of them veterans of World War I and World War II. At that time 86.5% of those veterans will be 45 years of age or older, as compared with only 22.8% of the living veterans today. In actual numbers there will be almost 14 million living veterans at or beyond the age of 45—more than three times as many as there are today. At that same time, in the year 1970, almost 13% of the living veterans will be age 65 or over, in comparison with only about 1% today. There will be an estimated 2,072,000 veterans age 65 or over—more than 10 times the present number.

The aging of our veteran population during the years and decades ahead will bring not only an increase in the total patient load in VA hospitals but also a marked rise in the number and proportion of non-service-connected cases. That fact is illustrated by a study showing the percentage of VA patients hospitalized for non-service-connected conditions as of Jan. 31, 1952. On that date civilian-incurred illness accounted for almost 54% of the World War II veterans, more than 80% of the World War I veterans, and almost 97% of the veterans of earlier wars. As veterans grow older and more vulnerable to chronic ailments, there is an increase in the average length of hospital stay, even for the same kind of illness. For example, an analysis of general medical and surgical patients discharged between July 1, 1945, and Dec. 31, 1950, showed that World War I veterans were hospitalized an average of about twice as long as World War II veterans who had the same kind of disabilities.

All of these facts and trends—past, present, and future—point to a tremendous future increase in the size and cost of the VA medical program, unless there is a change in the "come one-come all" policy regarding the treatment of non-service-connected cases. In 1945, five years before the Korean conflict, Gen. Frank T. Hines, then Administrator of Veterans Affairs, made the following prediction: "With the numbers involved in this war and with the needs clause retained in the legislation, a peak load requirement of some 400,000 beds by 1975 would seem a fair estimate. With the needs clause removed the number would be measurably increased to the extent that free hospitalization would be afforded by the government for approximately one-third of the adult citizens of the country, which in turn might involve a recurring annual expenditure for such item alone of approximately $1,000,000,000."

As pointed out in June, 1953, by the Washington research office of the Council of State Chambers of Commerce, in a study prepared for 31 state and regional chambers of commerce: "With a current veteran population of about 20 million growing by almost a million a year, it is time for the Congress and

organized veteran groups to reconsider their position with respect to legislation on behalf of the veterans. The time is not far off when veterans and their families will comprise the majority of our people and can no longer be considered a special-interest minority group. Attention of Congress and veterans' groups should, therefore, be directed increasingly to assisting veterans, including their survivors, whose disabilities or death are connected with military service, and to helping other truly needy veterans instead of providing special benefits to veterans as a class."

PLACEMENT OF PHYSICIANS IN MISSISSIPPI

During the summers of 1952 and 1953 the Council's Committee on Extension of Hospitals and Other Facilities employed medical students from Northwestern University Medical School to study the physician placement programs of a number of state medical associations. Descriptions of five of these programs, Ohio State Medical Association, Virginia Council on Health and Medical Care, Nebraska State Medical Association, Indiana State Medical Association, and Missouri Medical Association, were published in THE JOURNAL *on Feb. 21, 1953. The sixth and seventh in this series of articles, discussing the placement of physicians in Illinois and Texas, appeared in* THE JOURNAL *issues of Oct. 17, 1953, and Dec. 19, 1953. The following is the eighth state placement service described in this series of articles.*

The state of Mississippi has, for a number of years, been active in developing programs designed to cope with problems presented by poor distribution of physicians and hospital facilities. Examples of this activity are the placement services of the state Board of Health, of the Medical Education Board, and of the Mississippi State Medical Association.

This is the only state where three separate organizations have been prompted to assist communities in need of physicians and physicians seeking suitable locations in which to practice. The over-all benefit to Mississippi, derived from the efforts of these organizations, should not be underestimated. Their efforts have been a primary factor contributing to the increase in the number of physicians from 1,112 in 1946 to the present number of about 1,500, an increase of 35% in only eight years.

BOARD OF HEALTH PROGRAM FOR PLACEMENT

For many years communities in need of physicians and physicians seeking a location have requested information from the state Board of Health. From these requests has grown a simple system of exchange of information between communities and physicians. All of the requests from communities are assembled in a small booklet, *Places to Practice Medicine in Mississippi.* Twice each year the booklet is revised, omitting the communities that no longer need additional physicians and adding communities currently seeking physicians. This booklet, prepared by the division of maternal and child health of the state Board of Health, is distributed to all physicians who request information in regard to communities open for practice. Information about each location includes: the population of the area and town, the number of physicians, the physician-population ratio, the hospitals and their proximity to the location, and the name of the contact person. Prior to revision, a copy of the entry on each community in the booklet is sent to the local community sponsor so that the new booklet will contain the latest information on the opening.

During 1948, 1949, and 1950, the semi-annual editions of the booklet contained much additional information that was believed to be of interest to a young physician selecting a place to practice. The booklet included a section in which was analyzed the factors involved in deciding upon a location for practice. Next were tables on the number of physicians (by age groups—those under 40, those between 40 and 49, those between 50 and 59, and those over 60 years of age) practicing in each county. The method of determining the economic status of a community by comparing its sales tax collections preceded the statement of the sales tax collection in each county. Finally, a progress report of the Mississippi commission on hospital care on the construction and planning of hospitals in Mississippi showed extensive improvements that were being made and the additional facilities that would soon be available.

It was found, however, that only part of the information in the booklet was helpful to young physicians seeking a community location. Information about newly constructed hospitals in each county was found to be of special value. This information is available in the *Hospital Bulletin,* prepared and distributed by the Mississippi commission on hospital care. This publication is distributed to physicians in addition to the booklet *Places to Practice in Mississippi.* The reliability of the method of determining the economic status of a community was questioned. It was found more feasible to permit each young physician to make a personal investigation and gather his own information by direct contact with the community.

The decision as to whether a community is economically a good place to practice medicine depends upon a number of factors, including the physician's own ideas about income. To aid in this, the placement office follows three procedures. First, all young physicians are encouraged to visit the placement office of the state Board of Health in Jackson, where they have access to information supplementary to that contained in the bulletin *Places to Practice in Mississippi.* This information is secured for the placement office directly from communities desiring a physician by the county representatives of the state Board of Health. Secondly, if the physician wishes information in regard to tax payments and industrial activities, he is referred to the appropriate state agency, such as the state Tax Commission and the state Agricultural and Industrial Board. In this way the physician may secure up-to-date and detailed information, which the state Board of Health believes more effective than any material that it may publish. Finally, an effort is made to supply the physician with a community sponsor who will take an interest in him and will help him to gather such information as he wishes by an "on-the-spot" investigation of the community. This gives the young physician an opportunity to interview people in the community and to ask questions in regard to problems that will affect him directly.

To aid the communities requesting physicians, a complete list of all physicians who contact the placement office is prepared and mailed to the community sponsor. This facilitates the exchange of information between the community and the physician. From this point on, the physician and the community are expected to make the necessary arrangements. No attempt is made by the Board of Health to actively promote any individual community or physician. No follow-up is made to determine which physicians have located or which communities have secured the services of a physician.

PLACEMENT PROGRAM OF THE MEDICAL EDUCATION BOARD

Aiding Communities.—The Medical Education Board has been in a key position to render aid to the communities seeking physicians. Since its inception it has served as a clearing house for information, placing communities in contact with young physicians and young physicians in contact with areas in which they may serve the people of Mississippi who have made their education possible.

The medical education scholarship fund (described later) was established to supply physicians for small communities. The law requires that 75% of all recipients shall be placed in areas with a population of 5,000 or less. Due to the wide publicity that the loan fund has received in Mississippi, pointing to the Medical Education Board as a ready source of information concerning the supply of physicians, many communities have sought the aid of the board in obtaining a physician. At the time of a community's request for a physician, the inquirer is sent a list of all interns or doctors ready or nearly ready for practice assignment.

In a special listing that is sent to all loan awardees during their years of internship, the names of all such communities are compiled, together with information voluntarily supplied by the person or group of persons who originally made the request. To assure a personal contact in each community, the names of the persons to contact are included in the listing. In 1950, the board

distributed a pamphlet designed to inform communities of the procedure to be followed in securing aid from the Medical Education Board and to explain to them the responsibility each community must assume in attracting a physician and supporting him.

Aiding Loan Recipients.—In approving young physicians for practice in rural communities, the Medical Education Board follows a routine method of selection and approval designed to give the young doctor a choice of location, within the provisions of the law. The board supplies him with a list of communities that have signified a need for a doctor, including also a booklet containing pertinent statistics on these areas. This booklet, *Physician Population in Mississippi,* since first issued in January, 1949, has been used extensively by the loan recipients serving internships. The booklet contains a commentary on the current physician distribution problem and a tabulation of the ratio of physicians to total population in Mississippi, indicating the areas having no physician, the total number of physicians in each county, ratio of physician to population by county and by each rural area in the county, and the number of physicians, by county and by age—those over 60 and those under 40 years of age.

In addition to the booklet, the interns receive the *Mississippi Business Review* each month from the business research station of Mississippi State College. Progress reports of the Mississippi commission on hospital care are released to interns frequently, as well as printed brochures from the commission and the Agricultural and Industrial Board. In the office of the Medical Education Board, statistics on specific communities, prepared by the business research station of Mississippi State College, are available to loan recipients. All of this information is welcomed by interns and many of them have commented on its value to them. As a result, the state has a group of physicians, who, after considering the existing needs of the state, decide upon a place to practice in which they will be needed and satisfied.

When the doctor has made a choice of location, he informs the board and requests approval of the location selected. He lists the information that he has collected from the available publications and from personal visits to the community that has helped in his selection of the particular community. This report on the community of his choice is of value to the doctor because it requires considerable thought as to the desirability of the community from the standpoint of facilities available for home life as well as for his medical practice. It is also valuable to the board, enabling it to ascertain the need of the community and whether it qualifies for a physician educated from tax funds.

The board gives careful consideration to the physician's request, and, if satisfied that a doctor is needed at the location chosen, will approve the first choice. If neither the first nor the second choice is approved, the board reserves the right to assign the doctor to an area of its own selection. Thus far, however, no arbitrary decision as to location has been necessary.

PLACEMENT PROGRAM OF THE MISSISSIPPI STATE MEDICAL ASSOCIATION

In 1951, the president of the association suggested to the planning committee of the house of delegates that they consider the need and feasibility of a physicians placement service operated by the association. As a result of the study, they recommended "that the central office set up a bureau of placement, to coordinate information as to needs and opportunities for locations for doctors in this state. This bureau should work closely in cooperation with the local medical societies." Immediately the central office, under the direction of the executive secretary, Mr. Rowland B. Kennedy, began operating a clearing house for requests from communities and physicians. The medical association handles requests from physicians and from communities seeking physicians as individual cases, placing doctors and communities in contact without the formality of preparing published lists of physicians or communities.

In order to gain a clear picture of the problem that faced the new placement service of the medical association, Mr. Kennedy surveyed the data maintained on the membership cards of the association. The information obtained from this survey was plotted, first, by age group, then by distribution of physicians as to rural and urban practice, and, finally, by percentage of total population served by each group. A valuable adjunct to the survey was a study made in 1953 of the projected attrition of Mississippi physicians, by age group, for the next 10 year period, broken down into 5 year intervals. During the 10 year period, attrition by death with no resupply calculated would reduce the present ranks of physicians from 1,497 to 1,377. Thus the Mississippi State Medical Association had a picture of what to expect for planning purposes in its placement program. The outstanding problem facing the placement service is to replace the older physicians as they limit their practice or retire, to increase the supply of young physicians for rural areas, and ultimately to increase the total number of physicians practicing in the state as the demand for more medical doctors increases.

Requests from Physicians.—The placement service aids all physicians who seek its assistance. About 80% of the requests from physicians come to the office through the mails from various sources of referral, and 20% are received by means of personal visits to the office. Referrals are from other state medical associations, the Physicians Placement Service of the American Medical Association, the state Board of Health of Mississippi, and the county societies. Upon receipt of a request, the identity of the physician is ascertained by checking the Directory of the American Medical Association. If the writer is not in the Directory and was not referred to Mississippi by the A. M. A. Physicians Placement Service, the identity of the writer is checked through the A. M. A. and by his references and credentials. Mr. Kennedy then writes a personal letter to the physician answering any specific questions asked and requesting information on his educational background, licenses, interests as to type of practice desired, and other pertinent data. If the physician has requested information about a specific location, the personal letter that he receives will contain information on the population of the town, its major source of revenue, a description of the geographical area, information on types of transportation—highways, bus and rail connections, and air lines—as well as the number and ages of doctors already in practice in the community; also included are data on schools, churches, goods and services, hospital and clinical facilities, housing, a statement on the economic outlook of the community, and the names of resident physicians and county medical society officers.

Each month the placement service publishes a selected list of physicians who have expressed a desire to locate permanently in the state. This list is included in a bulletin that is distributed to association members. Only the names of those physicians who will be immediately available are published. If a physician is in his internship and will not be available for six to eight months, his name will not be published until he is available.

At the end of the internship period each year, the Medical Education Board has 40 to 60 young physicians available to assign to rural communities. At this time, the placement service of the medical association writes to the out-of-state physicians who are not participants of the scholarship program and suggests that, although at the present time, there are no apparent openings in the state, if the physician is still interested in finding a location in Mississippi six months hence, he should contact the placement service again at that time.

Requests from Communities.—The placement service tries to assist communities requesting aid in direct proportion to their individual circumstances. The service is informed of a location for a physician by local communities desiring aid in securing a physician, the local medical society, the surveys conducted by the state Board of Health, and the committee on the doctor draft of the association.

When the Placement Office is informed of the need for a doctor, the name of the community is referred to the local medical society. Members of the county association visit the community and talk to the inhabitants personally. Because the placement of a physician is so important, each community is given thorough consideration and the problems carefully reviewed. Instead of sending a questionnaire to gather information on the hospitals,

the sources of income of the community, the number of physicians, and other pertinent data, Mr. Kennedy refers to sources of information that he considers much more accurate than the type of information derived from a questionnaire. The sources used most are *The Hospitals Registered by the American Medical Association 1952 Census of Hospitals, reprinted from* THE JOURNAL; the *Curtis Marketing Index, Census of 1950,* used to determine the population figures for the community, county, and surrounding area; and listings in the office of the state medical association, used to determine the age and scope of activities of local physicians. Mr. Kennedy determines the position of the community in the primary medical service area and its proximity to the prime-primary medical service centers by consulting the publications of the American Medical Association on medical service areas. By personal contact through the local medical society, the existing or projected office facilities, as well as housing already present in the community, is investigated. This thorough-going procedure is possible because, according to the executive secretary of the state association, the number of communities in Mississippi without a physician is statistically insignificant.

The placement service maintains a file of the correspondence both from physicians and communities. As a cross check to determine when a location has been filled or a physician has located in the state after corresponding with the placement office, the office uses several methods. The state Board of Medical Examinations informs the placement service of the entire list of physicians who have been licensed to practice in Mississippi. Letters from the secretaries of the county medical societies or from the councilors of the state association and from the county health officer all come to the placement office carrying information about newly located physicians and recently filled locations.

A rough evaluation of the benefit Mississippi derives from the activities of the Placement Service of the Mississippi State Medical Association can be gained from the statistics of physicians placed and locations filled. During the past calendar year, the state association office serviced more than 50 individual cases. Actual placement runs only about 20% of total cases serviced, for a physician desiring a permanent location is usually negotiating with several states in a given geographical area. However, about 15 physicians were given personal help in finding a suitable location, and about 20 communities were investigated thoroughly and aided directly by Mr. Kennedy in securing a physician. These figures are outstanding in the face of the activities of the Medical Education Program, which provides a constant and predictable supply of general practitioners obliged to fill the needs of small communities and placed there by the Medical Education Board.

The future plans of the placement office are extensive. Mr. Kennedy plans to "continue to make the Physicians Placement Service program as constructive as possible in furtherance of the objective of the best medical care for all in a climate of free enterprise and personal choice of physicians. The Medical Association will expand or decrease the Physicians Placement Service as the best interests of the State appear."

OTHER RELATED PROGRAMS

Scholarship Program.—The legislature of January, 1946, established a medical education scholarship program for the purpose of obtaining general practitioners for the small communities and, in doing so, help deserving Mississippi medical students meet the cost of medical education.

The state supported scholarship program provides grants of $1,250 annually for four years to residents of the state who have completed premedical training and have been accepted by any class A medical school. The student agrees to practice a minimum of two years in a rural area approved by the state Medical Education Board. The loan is repaid by service, each year of practice in the designated area reducing the loan by one-fifth. Since the scholarship program was initiated, no white or Negro medical student who was qualified to enter a class A medical school has been denied that opportunity for lack of money. As of July, 1953, 406 Mississippi students, including 30 Negro students, have been aided by the program. Of the group receiving aid, 12 are women. In the fall of 1953, 259 were still attending medical school or were in hospital internships, while about 160 had returned to Mississippi and were in private practice. These are located in communities that have an average population of around 2,000. Until the new medical school and teaching hospital are ready to receive students, scholarships in medicine and also in nursing are available under the Medical Education Board program. In the future, Mississippi can expect an annual supply of 50 physicians through this program. Since the attrition by death has averaged 40 physicians per year for the past six years, the scholarships alone will more than offset the loss.

Hospital Construction.—The state was quick to act upon the Hospital Survey and Construction Act of the 79th Congress and developed an aggressive program to meet its hospital needs. This program, under the commission of hospital care, has now achieved about one-half of its original objective. Fifty hospitals have been completed, are under construction, or have had plans approved for construction. Many of them are small, 25-to-50 bed hospitals, which together with the other hospitals will bring these needed facilities within about 20 miles of every home in the state. A total of 2,073 beds have been added to the state, raising the total of 4,200 in 1946 to 6,270 in 1953.

The county health department program has also added to the medical resources of Mississippi, especially in rural districts. Fifty buildings have been completed or are planned. In towns where office space suitable for carrying on a modern medical practice was not available, space was provided in the new health center buildings. These offices, in which local physicians carry on their practice, are equipped with modern x-ray apparatus and a small clinical laboratory. Such facilities apparently have been a favorable factor in getting physicians of the desirable group into the communities that have the greatest need for young active physicians. In 1951, 48 physicians with an average age of 34 years located in towns having an average population of 2,100.

Medical Education.—The state participated in the organization of the Southern Regional Education group in 1948. This group provides that students from one state may be sent to the schools in participating states for specialized training in subjects not provided for in the home state. The schools giving the service are remunerated for their over-all teaching expense by the state in which the students live. Under this program, $409,000 has been spent since 1949, with 241 students enrolled for varying periods in medical schools under regional contracts from Mississippi.

The growing need for a four-year school was recognized by the state legislature in 1950 when it appropriated the initial funds for the construction of the school and teaching hospital. The dedication and ground-breaking for the new, 9 million dollar, four-year medical school and teaching hospital took place in Jackson, Mississippi, on December 5, 1952. These facilities will be the principal source of physicians in the future. The school will have a capacity for 320 students when it opens in 1955 and hopes to reach an enrollment of 400.

To assist the medical profession by relieving the nursing shortage, the state of Mississippi established a department of nursing at the University of Mississippi in the fall of 1948. The state established a scholarship fund for graduate nurses to be used for advanced study in nursing education; by this means, teachers are to be provided for the new department. The maximum grant per student is $3,000, to be used in attending any school giving the necessary courses. In return, the student promises to serve as an instructor in the state's schools of nursing one year for each year of scholarship. Each year's service as an instructor reduces the debt by $1,000.

Tulane University of Louisiana School of Medicine, in a program sponsored by the state of Mississippi, has two part-time consultants in pediatrics and obstetrics in the field, who consult with local Mississippi physicians and establish programs for maternal and child health. The school also has a consultation service for physicians in these rural areas. As part of its teaching program, Tulane University of Louisiana School of Medicine rotates residents through rural hospitals in Mississippi.

MEDICAL MOTION PICTURES

MEDICAL MOTION PICTURES

The following excerpt from a letter from the attestation officer of the U. S. Information Agency will be of interest to physicians and others who are asked to loan medical motion pictures to colleagues in foreign countries.

"Many producers and distributors of medical motion pictures have been reluctant to loan or rent their films abroad because of the complicated procedures and numerous forms necessary to secure their return through American customs. Recent modification of customs procedures have made it possible to clear films on their return, with the use of but a single form, which should accompany the shipment when it leaves this country. The new procedure is as follows:

"(1) Obtain Customs Form 3311 from the U. S. Customs Office in your area before you ship the film.

"(2) Fill out and execute the form, making following statement in the REMARKS section:

'It is requested that all other forms required by section 10.1 of the regulations be waived. These films contain no obscene or immoral matter, nor any matter advocating or urging treason or insurrection against the United States or forcible resistance to any law of the United States, nor any threat to take the life of or inflict bodily harm upon any person in the United States.'

"(3) Affix the form to the outside of the film can or container in an envelope marked 'Documents for U. S. Customs.' Tell the consignee to see to it that the form is still on the can WHEN THE FILM IS RETURNED.

"The Customs Officer at the port of entry will remove the form when the film is returned, and find on it all the information he needs to enable him to admit the film duty-free.

"The procedure applies to motion pictures valued at not to exceed $250."

BUSINESS PRACTICE

The following material is based on a public relations manual issued by the Public Relations Department of the American Medical Association.—ED.

USE OF THE TELEPHONE

Like an extra arm to the physician is that wonderful but pesky invention—the telephone. It is an instrument, however, that requires special handling. During the doctor's office hours the telephone should never be left unattended. If there is only one assistant and she must leave her desk, she should alert the doctor so that he may answer it until she returns. A pad and pencil should always be beside the telephone so that all messages can be jotted down. The person answering the telephone should identify himself. The doctor's receptionist should say: "Dr. Smith's office, this is Miss Larson, the receptionist, speaking."

Courtesy should be a telephone byword in the physician's office. Each caller should be welcomed as warmly over the telephone as in person. The impression of being hurried when on the telephone should be avoided. The physician's voice should convey cheerfulness, interest, and friendliness in order to establish cordial patient relations at once. The placement of the telephone is important in a doctor's office. It is bad taste to talk over the patient's problems in front of an office full of patients. There is a muffler attachment into which one can speak without others present in the room being able to hear what is said. The doctor's receptionist should be warned against telephone indiscretions. The mere repetition of the patient's name over the telephone when other patients are listening can be unwise, especially if the doctor's specialty gives away the nature of the patient's condition.

Emergency calls require special attention. When the doctor is out of the office and an emergency call comes in, his assistant should find out who is calling, the address, the nature of the emergency, directions on how to reach the patient, the patient's condition, the telephone number of the person who called, and other details. The doctor should keep his home or his office informed of his whereabouts so that he can be reached immediately. It is also a good idea for the physician or his assistant to make a follow-up telephone call inquiring about patients whose condition does not necessitate another visit; the doctor might also say, when dismissing such a patient: "Call me in a day or two and let me know how you feel," or "Please be sure and let me know if you don't feel better." Such calls show the doctor is sincerely interested and cut down on unnecessary second visits.

It is important to avoid constant telephone interruptions. Sometimes, just as a patient is about to make a statement that has an important bearing on his case, the telephone rings. By the time the doctor has completed the call, the patient may have changed his mind about making the statement. Every physician should have an understanding with his assistant about telephone interruptions. If possible, the assistant should find out whether the call is an emergency; if not, the physician can call back at his convenience. There can be no hard and fast rules laid down about calls to the doctor, however. Sometimes a word of assurance from him is all that is needed at the moment. A patient has a right to talk to his physician and cannot always be headed off by an assistant. If the telephone is wisely used, it will work for the doctor.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Income Taxes: Physician's Liability for Penalty for Underpayment.—The plaintiff filed suit to recover fraud penalties assessed against him for underpayment of his federal income tax. From an adverse judgment in the trial court, the plaintiff appealed to the United States Court of Appeals, Eighth Circuit.

It appeared from the evidence that for the years 1944, 1945, 1946, and 1947, the tax liability reported by the plaintiff on his income tax returns was $13,150.99. His actual tax liability during that period was $49,365.03. He had underpaid his taxes in 1944 by $10,119.69, in 1945 by $11,219.83, in 1946 by $5,393.63, and in 1947 by $9,480.89. Deficiencies and fraud penalties were assessed against the plaintiff. He paid the deficiencies, including the penalties, but then filed this suit for a refund of $16,296.34, on the ground that the deficiencies had resulted from negligence "without intent to defraud" and that the assessment of penalties in excess of 5% of the deficiencies was unlawful. The taxpayer testified that the inaccuracies in his income tax returns for the years in suit were not the result of any intent to evade his taxes but were caused by the stress of his professional work as a physician and surgeon (due to the shortage of doctors in the community that he served) and by his having inexperienced office help.

The district court regarded the taxpayer's explanation as inadequate and unconvincing. We think, said the Court of Appeals, that in an action such as this, when it appears that an intelligent taxpayer with a substantial income, readily ascertainable, has, for a period of several years, made income tax returns that seriously understate his true taxable income and tax liability, the question whether the resulting tax deficiencies were the result of negligence or of fraud on his part is a question of fact to be determined by the trial court. The question of intent, if at all doubtful, is ordinarily one of fact for the trier of the facts. One may be presumed to intend the natural and necessary consequences of his acts. The taxpayer's returns for the years in suit were concededly false. The question whether they were also fraudulent and made with intent to evade taxes, has, said the Circuit Court of Appeals, been conclusively determined by the trial court.

Accordingly the judgment of the trial court against the plaintiff was affirmed. *Owens v. United States, 197 F. (2d) 450 (1952).*

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Dermat. and Syphilol., Chicago

69:1-132 (Jan.) 1954

Undergraduate Instruction in Dermatology: Critique. H. S. Alden, J. W. Jones and P. H. Nippert.—p. 1.
Pitfalls in Diagnosis and Treatment of Melanoma. S. W. Becker.—p. 11.
*Reddish-Orange Fluorescence of Necrotic Cancerous Surfaces Under Wood Light. F. Ronchese, B. S. Walker and R. M. Young.—p. 31.
Comparative Effects of Neomycin and Other Antibiotics on Pyogenic Bacteria: In Vitro Effect on Bacteria Isolated from Cutaneous Pyogenic Infections. C. S. Livingood, C. E. Head, R. M. Sutter and F. B. Engley Jr.—p. 43.
Association of Mucocutaneous and Visceral Cancers. E. Epstein.—p. 58.
*Treatment of Pemphigus with Cortisone by Mouth. A. H. Conrad Jr., J. Greenhouse and R. S. Weiss.—p. 66.
Sodium Sulfacetamide in Topical Therapy. W. W. Duemling.—p. 75.
Chromoblastomycosis: Report of Nine Cases from Single Area in Louisiana. J. K. Howles, C. B. Kennedy, W. H. Garvin and others.—p. 83.
Effect of Treatment in Late Latent Syphilis. C. W. Barnett, N. N. Epstein, A. F. Brewer and others.—p. 91.

Fluorescence of Necrotic Cancerous Surfaces Under Wood Light.—Ronchese and associates point out that Wood in 1903 utilized ultraviolet radiations passed through a nickel oxide filter to remove visible light. This invention has proved useful in medicine and many other fields and in the diagnosis of the ringworm of the scalp and a number of other dermatological disorders. In reviewing the use of the Wood light in the study of cancerous surfaces, the authors mention the peculiar fluorescence of epidermoid carcinoma, in contrast with basal cell carcinoma, as observed and discussed in France 20 years ago. No further investigation of this particular phase of fluorescence has since appeared in the literature. They assume that the reasons are, first, that the biological factors remained unknown and, second, the lack of demonstrative color illustrations. They obtained material for bacterial investigation from four patients with advanced carcinoma showing reddish-orange fluorescing areas under the Wood light. No red fluorescence or an uncertain fluorescence was elicited in cultures, and no difference was noted in the organisms obtained in fluorescing and nonfluorescing areas. Further investigations in one of these cases, however, resulted in the isolation of a micro-organism that can be shown to produce a similar fluorescence under laboratory conditions. This organism is not properly a bacterium, but has the characteristics of the genus Streptomyces. The fluorescence that is bright red occurs only when this organism is grown on a culture medium that contains blood. The authors hope that further studies will clarify the relation of this organism to the peculiar fluorescence. While the phenomenon has been discussed in the past, this is the first time that satisfactory color photographs were obtained. The authors conclude that the peculiar vivid reddish-orange fluorescence elicited by the Wood light from necrotic ulcerated surfaces of squamous cell epitheliomas, in contrast to the uniform deep violet discoloration of other ulcerated surfaces (basil cell epithelioma, carbuncle, tubercular and syphilitic gumma, granuloma fungoides, pseudoepitheliomatous hyperplasia, and long-standing inflammatory process), is valuable in ruling out the above-mentioned conditions and considering the clinical diagnosis of epidermoid (squamous cell) carcinoma. The red fluorescence was regularly observed in open, necrotic adenocarcinomas of the breast and in one case of facial fibrosarcoma. It is not known what part adenomatous, sarcomatous, or epidermal cells play in the production of the red fluorescence. The only fact known is that for a lesion to elicit the fluorescence it must be a cancer, ulcerated, necrotic, and highly malignant.

Cortisone Given Orally in Treatment of Pemphigus.—Conrad and his associates treated, with oral administration of cortisone, five patients with pemphigus vulgaris, 2 with pemphigus erythematosus, and one with pemphigus foliaceus. With the exception of the case of pemphigus foliaceus, in which treatment with cortisone by mouth produced little or no effect, the clinical response to oral therapy closely paralleled the response to the parenteral use of the drug. Laboratory findings likewise indicated that the responses to the oral use of cortisone are about the same as to its parenteral administration. Somewhat larger oral doses seem to be necessary for the control of the disease. The ease of oral administration of cortisone makes it the treatment of choice for pemphigus. Cortisone does not cure pemphigus, it merely controls its symptoms, and, as in arthritis, maintenance therapy must be continued indefinitely. Toxic phenomena can be kept under control with careful observation.

A.M.A. Arch. Ind. Hyg. & Occupat. Med., Chicago

9:1-88 (Jan.) 1954

Studies of Phosphorus Intoxication: 1. Changes in Blood, Urine, and Tissues of Dogs Poisoned with Phosphorus. D. J. Buchanan, M. V. Sigal Jr., C. S. Robinson and others.—p. 1.
Comparative Exchange of Calcium, Lead, and Radioactive Lead in Dogs. J. A. Calhoun, R. McLean, J. C. Hudson and J. C. Aub.—p. 9.
Participation of Labor Union in Study of Problems of Psychiatry in Industry. L. L. Tureen.—p. 23.
Toxicity of Silica: II. Characteristics of Protein Films Absorbed by Quartz. L. D. Scheel, B. Smith, J. van Riper and E. Fleisher.—p. 29.
Physiological Responses to Parathion Exposure: Correlation Between Serum Cholinesterase Activity and Urinary Paranitrophenol Excretion R. K. Waldman, J. Lieben and L. Krause.—p. 37.
Comparative Toxicity of Two Vinyl-Substituted Phosphates. J. K. Kodama, M. S. Morse, H. H. Anderson and others.—p. 45.
Two Chambers for Use in Exposing Laboratory Animals to Inhalation of Aerosols. E. C. J. Urban.—p. 62.
Efficiency Studies of Electrostatic Precipitator. K. E. Lauterbach, T. T. Mercer, A. D. Hayes and P. E. Morrow.—p. 69.

A.M.A. Arch. Ophthalmology, Chicago

51:1-146 (Jan.) 1954

Ascorbic Acid in Aqueous Humor and Serum of Patients With and Without Cataract: Physiologic Significance of Relative Concentrations. E. F. Purcell, L. H. Lerner and V. E. Kinsey.—p. 1.
Ocular Antibiotic-Producing Bacteria in Normal Eyes and in Conjunctivitis. S. P. Halbert, L. Swick, C. Sonn and D. Locatcher-Khorazo.—p. 7.
Visual Effects of Pink Glasses, Green Windshields, and Glare Under Night-Driving Conditions. P. W. Miles.—p. 15.
Study of Compensation-Maximum Test on Aqueous Veins. J. L. Stambaugh, J. C. Fuhs and K. W. Ascher.—p. 24.
Recession Under Tenon's Capsule. K. C. Swan and T. Talbot.—p. 32.
Electroretinography in Circulatory Disturbances of Retina: II. Electroretinogram in Cases of Occlusion of Central Retinal Artery or of One of Its Branches. H. E. Henkes.—p. 42.
Id.: III. Electroretinogram in Cases of Senile Degeneration of Macular Area. H. E. Henkes.—p. 54.
Spontaneous Hole in Anterior Hyaloid Membrane. J. Laval and R. Collier.—p. 67.
Mandibulofacial Dysostosis. P. Hurwitz.—p. 69.
*Retrolental Fibroplasia: Definitive Role of Oxygen Administration in Its Etiology. J. C. Locke.—p. 73.
Uveitis in Children. S. J. Kimura, M. J. Hogan and P. Thygeson.—p. 80.
Beryllium and Delayed Corneal Healing: Report of Case. G. Flynn and M. Raiford.—p. 89.
Lids, Lacrimal Apparatus, and Conjunctiva. A. E. Braley.—p. 91.

Retrolental Fibroplasia: Oxygen Administration in Its Etiology.—Locke points out that in July, 1951, Campbell of Australia published observations on a series of cases of retrolental fibroplasia that suggested that the disease might be due to excessive administration of oxygen. Since this time, Campbell's experiences have been shared by several investigators in different

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Titles marked with an asterisk (*) are abstracted.

parts of the world. However, in December, 1951, and again in March, 1952, the opposing view was propounded by Szewczyk of St. Louis, namely that the disease was due to anoxia and that oxygen not only could prevent the disease but also would be effective in its therapy. The studies reported by Locke were carried out in 1951 in the nurseries of two New York hospitals and, since early in 1952, in the premature nurseries of two Montreal hospitals. A correlation between the incidence of retrolental fibroplasia and the duration of continuous oxygen therapy was demonstrated in comparative studies on 327 premature babies. When the oxygen being administered routinely to premature babies was reduced to minimal amounts, there was a striking fall in the incidence of this disease. It occurred in only 2 out of 124 babies, and both cases were mild. On the basis of previous experience, 32 cases would have been expected to occur in a population with this birth weight distribution. Babies in whom the disease developed received, on the whole, significantly more oxygen than those in whom it did not develop, although the relationship is not an absolute one. The disease seems to be directly related to hyperoxia, rather than to any secondary anoxia induced by oxygen withdrawal. Whether rapid removal from high oxygen can increase the tendency toward retrolental fibroplasia cannot be deduced from this study.

A.M.A. Arch. of Surgery, Chicago

68:1-134 (Jan.) 1954

Use of Controlled Hypotension in Large Blood Vessel Surgery. W. W. L. Glenn, L. J. Hampton and A. V. N. Goodyer.—p. 1.

Gastrointestinal Bleeding Due to Splenic Vein Obstruction by Pancreatic Tumors. E. S. Hurwitt, S. F. Altman, G. R. Gerst and B. M. Webber.—p. 7.

Physiologic and Surgical Considerations in Treatment of Complicated Lesions of Biliary Tract. W. Walters.—p. 12.

*Intestinal Antisepsis with Oxytetracycline (Terramycin) and Neomycin: Comparative Study. W. G. Anlyan, D. Hart, N. G. Georgiade and M. A. Poston.—p. 28.

Clinical Trials of New Plastic Dressing for Burns and Surgical Wounds. D. S. J. Choy.—p. 33.

*Treatment of Surgical Shock with Arterenol. R. E. Fremont, N. M. Luger, S. N. Surks and A. Kleiman.—p. 44.

Experimental Repair of Ureters by Polyethylene Tubing and Ureteral and Vessel Grafts. C. A. Hardin.—p. 57.

Present Status of Carcinoma of Pancreas. W. B. Hutchinson.—p. 62.

Effect of Streptokinase-Streptodornase on Peritoneal Talc Adhesions and Granulomas: Experimental Study. E. M. Luttwak, J. D. Feldman and Z. Neuman.—p. 69.

Protein Nutrition in Surgical Patients: I. Time Factor in Protein-Sparing Action of Dextrose in Parenteral Feeding. R. D. McNair, D. O'Donnell and W. Quigley.—p. 76.

Surgical Significance of Marginal Mandibular Branch of Facial Nerve. R. S. Pollack.—p. 81.

Retropubic Approach to Bladder Neck Resection in Children. M. C. Wilson, G. R. Horton, B. F. Horton and J. W. Byrne.—p. 87.

Whole Body Irradiation on Healing of Fresh Fractures. A. W. Spittler, J. W. Batch and B. A. Rutledge.—p. 93.

Oxytetracycline vs. Neomycin.—A comparison was made of the efficacy of oxytetracycline (Terramycin) and neomycin in the antiseptic preparation for surgery of the colon and rectum. Oxytetracycline was given to 22 patients in a dosage of 500 mg. every 6 hours for 48 to 54 hours and to 7 patients in a dosage of 750 mg. every 6 hours for 48 to 54 hours. Neomycin, 1 gm. every 4 hours for 72 hours, was given to 10 patients, and 12 patients received 2 gm. of it every 4 hours for 48 hours. Oxytetracycline reduced the intestinal bacterial count without any marked change in the floral spectrum, whereas neomycin inhibited the growth of almost all bacterial flora of the intestine. The growth of Escherichia coli and streptococcic organisms was totally inhibited by neomycin, while oxytetracycline failed to change the incidence of positive cultures of Streptococcus faecalis among preoperative and postoperative specimens from the patients treated with it. The cultures of 9 out of 20 patients remained positive for E. coli after the administration of oxytetracycline. The authors conclude that neomycin is the drug of choice for intestinal antisepsis. Bacterial inhibition is more complete with it than with oxytetracycline; the side-effects of the two drugs are essentially the same.

Arterenol in Surgical Shock.—The authors used continuous intravenous infusions of levarterenol (Levophed) in the treatment of 22 cases of surgical shock and 10 cases of neurological shock. Of the cases that are of surgical interest, 6 were associated with an acute surgical abdominal condition, 12 occurred during or after major operative procedures, 3 of these were associated with a considerable loss of blood in each case, and 4 were cases of severe hemorrhagic shock. It is felt that the indications for use of a pressor substance such as levarterenol ought to be widened in view of the fact that it constantly showed itself capable of elevating blood pressure and often brought patients out of shock when it was added to fluid replacement therapy that in itself had been ineffective. It was successful in reversing the state of shock in three out of four patients with hemorrhagic shock, a condition that has been regarded as not amenable to vasopressor therapy. The use of levarterenol made it possible for some patients in profound shock to undergo extensive, sometimes lifesaving, surgical procedures. The response of the blood pressure and the pulse rate are the best guides to the efficacy of this drug. It is essential that the cause of shock be discovered prior to or early in the course of treatment lest a hidden hemorrhage result in death.

American Heart Journal, St. Louis

46:799-952 (Dec.) 1953

Studies of Effect of Second Degree of Freedom in Ballistocardiography. J. E. Smith and R. Rosenbaum.—p. 799.

RS-T Segment Elevation in Mid- and Left Precordial Leads as Normal Variant. M. J. Goldman.—p. 817.

Spatial Angle Between Long Axis of QRS Loop and Longitudinal Axis of Ventricles. N. O. Fowler Jr. and R. A. Helm.—p. 821.

Sequential Electrocardiographic Changes Following Auricular Injury. T. N. James and T. Geoghegan.—p. 830.

Auriculoventricular Nodal Rhythm with Heart Block. R. J. Vakil.—p. 844.

Pressure Patterns from Coronary Venous System in Man. G. Miller, B. M. Kaplan and L. N. Katz.—p. 852.

*Toxic Effects of 1-Hydrazinophthalazine in Ambulatory Hypertensive Patients. M. H. Wald, M. I. Ferro and K. H. Keeton.—p. 861.

*Anticoagulants in Treatment of Cardiac Infarction. A. J. Kerwin.—p. 865.

Effects of Thiamin Deficiency on Myocardial Metabolism in Intact Dogs. D. B. Hackel, W. T. Goodale and J. Kleinerman.—p. 883.

Primary Cardiac Amyloidosis. A. I. Thomashow, W. D. Angle and T. G. Morrione.—p. 895.

Transmission of Electrocardiographic Signals over Telephone Circuits. E. G. Dimond and F. M. Berry.—p. 906.

Effects of 1-Hydrazinophthalazine (Apresoline) in Hypertensive Patients.—Most published data on hydralazine (Apresoline) have been concerned with studies of hospitalized hypertensive patients. Since the majority of hypertensive patients must be treated as ambulatory outpatients, Wald and associates selected such patients for study. Of 12 patients who had been followed in the outpatient clinic of the Evanston Hospital for from 1 to 13 years, severe substernal pain, slight nausea, headache, and coldness developed eight hours after taking a single dose of 25 mg. of hydralazine in one who had asthma and angina pectoris. The drug was not given again, and the case was not included in the series. The duration of therapy in the remaining 11 patients was from 4 to 16 weeks, and the dosage ranged from 150 to 500 mg. daily in divided quantities. Dosage was begun at 12.5 mg. three times daily (after the initial disquieting experience with the single 25 mg. dose noted above). This was gradually increased to the point of tolerance. The usual division of dosage was either three or four times daily, whichever proved most effective. The blood pressure was measured three times weekly during the first weeks of therapy and then once a week until discontinuance of the drug. Digitalis, low sodium diet, and ammonium chloride were continued during the trial period in one patient, since he had been on this regimen for years. Aside from the continued use of phenobarbital by three patients and the occasional use of aspirin by others, no medication other than hydralazine was given. Of the 11 patients, only 2 had significant lowering of blood pressure. In all others the hypotensive effects noted during treatment were not greater than could be accounted for by spontaneous fluctuation. Toxic side-effects were observed in all, being fairly severe in eight and ultimately intolerable in three of these.

Anticoagulants in Cardiac Infarction.—Kerwin reviews 220 patients with cardiac infarction treated with bishydroxycoumarin (Dicumarol) and 81 treated with phenindione (Danilone). The control series was made up of 160 patients comparable in age and sex distribution. The mortality rate in the control series was 29.4% and in those treated 17.9%. The most marked

difference was in patients over 60 years of age. Where previous evidence of coronary disease (angina and/or infarction) existed, the mortality in controls was 30% and in treated 20.5%. Where no such diagnosis had been made before, the mortality rates were 25.9% and 15.7% respectively. The mortality rate in hypertensives was not affected by treatment, but in non-hypertensives it was 32.9% in the controls and 14.2% in the treated. Diabetic patients showed a much improved death rate with anticoagulants, but the number of cases was small. In those patients who had no cardiac failure, there was no difference in the death rate between treated and untreated patients. In the presence of cardiac failure, anticoagulant therapy was associated with a decrease in the death rate from 60.6% (controls) to 33.3% (treated). Thromboembolic complications occurred in 20% of the controls and in 7.6% of those receiving anticoagulants. These differences were evident only in patients over 50 years of age and were marked mainly after the second week of treatment. In those treated with anticoagulants, hemorrhagic complications, mostly in the urinary tract, occurred in 18.6%. Bleeding was much less common with phenindione than with bishydroxycoumarin. The author feels that the natural course of patients with cardiac infarction is by no means clearly established, and this fact makes the evaluation of therapy difficult. Controversy has arisen as to whether anticoagulant treatment actually does reduce morbidity and mortality rates. There is also a difference of opinion whether all patients should be routinely so treated, or whether only those with complicated cases (poor risks) require anticoagulants. The present study cannot settle these questions. The results suggest that anticoagulant therapy does influence the outcome favorably, most strikingly in patients with cardiac failure, especially in the older age groups.

American Journal of Medical Sciences, Philadelphia

227:1-116 (Jan.) 1954

*Placental Transmission of Lupus Erythematosus Factor. R. G. Bridge and F. E. Foley.—p. 1.

Relapse of Vivax Malaria Treated with Primaquine and Report of One Case of Cyanosis (Methemoglobinemia) Due to Primaquine. J. E. Hansen, E. A. Cleve and F. W. Pruitt.—p. 9.

Spontaneous Pneumothorax. M. R. Jones and H. A. Lyons.—p. 13.

Re-Evaluation of Etiology of Postarsphenamine Jaundice. D. G. Pocock.—p. 21.

*Paroxysmal Nocturnal Hemoglobinuria: Report of Case with Rare Hemoglobinuria Treated with Corticotropin. H. Fudenberg, W. L. Palmer and J. B. Kirsner.—p. 32.

Fundamental Problems in Jet Injection. W. W. Coon, P. E. Hodgson and D. L. Hinerman.—p. 39.

Superior Vena Cava Syndrome. M. M. Schechter.—p. 46.

*Use of Apresoline in Hypertensive Arteriosclerotic Syndrome. J. Kleh and J. F. Fazekas.—p. 57.

Effect of Potassium Depletion Induced by Desoxycorticosterone Acetate on Lethal Dose of Lanatoside C in Dogs: Relationship of Plasma Levels, Skeletal and Cardiac Muscle Potassium Content to Lethal Dose. S. Zeeman, S. Hirsch and S. Bellet.—p. 65.

Long Term Treatment of Rheumatoid Arthritis with Para-Aminobenzoic Acid and Cortisone Acetate. L. L. Wiesel and A. S. Barritt.—p. 74.

Effect of Para-Aminobenzoic Acid on Metabolism of Cortisone in Liver Tissue. L. L. Wiesel.—p. 80.

Observations on Diuretic Response to Parephyllin (R-3588), Neohydrin and Mercuhydrin when Administered Alone and in Combination. M. C. Silverthorne and J. H. Moyer.—p. 83.

Lupus Erythematosus Factor.—The LE (lupus erythematosus) phenomenon was demonstrated in the newborn of a mother with disseminated lupus erythematosus. The presence of the LE phenomenon in the baby was considered to be the result of placental transmission of the LE factor. Evidence was equivocal but suggestive that the LE phenomenon was still demonstrable in the baby seven weeks after delivery. It was definitely absent four months after delivery. By the methods used (precipitation and neutralization) there was no evidence of production of antibodies against the LE factor in the baby. The action of the placental barrier is not well understood. If, as seems likely, the placental membranes act only as an ultrafilter, then the LE factor probably existed in the maternal circulation as a simple gamma globulin and not combined with any molecule of very large size. The authors do not believe that the presence of the LE phenomenon in this baby means that the child has now or will develop disseminated lupus erythematosus. It is more likely that the LE factor is a part of the disease process and that it can be transmitted across the placental barrier without producing the disease in the baby. Since this paper was submitted for publication, the authors studied another pregnancy in a woman with disseminated lupus erythematosus. The LE phenomenon was demonstrable in the umbilical cord blood.

Paroxysmal Nocturnal Hemoglobinuria.—A case of paroxysmal nocturnal hemoglobinuria or Marchiafava-Michelli syndrome in a 26-year-old woman is described. The diagnosis was not made until two years after the onset of the clinical manifestations of the disease, because hemoglobinuria was not a symptom. The chief manifestation was attacks of severe abdominal pain recurring every two or three weeks. A tentative diagnosis was finally made on the basis of this recurrent pain plus the following hematological picture—normocytic anemia with reticulocytosis, leukopenia, and marrow findings suggestive of hemolysis (erythroblastic hyperplasia with increased storage of iron), with only borderline elevation of the serum bilirubin and fecal and urinary urobilinogen. Laboratory studies determined hemosiderinuria and an abnormal tendency of the erythrocytes to hemolysis. The experimental administration of 2 gm. of aspirin at bedtime, in an attempt to produce increased hemolysis by minimal acidification of the blood, resulted in increased hemosiderinuria in the morning urine, thus confirming the diagnosis. A program of corticotropin therapy was carried out with remarkable success in this patient. The daily dosage was varied according to the patient's changing requirements and the degree of discomfort from the side-effects of corticotropin. An attempt was made to strike a balance between underdosage with minimal symptoms and overdosage with Cushing's syndrome. The schedule was eventually stabilized to 40 units of corticotropin every third day. This therapy apparently caused a remission of symptoms of at least six months' duration, prevented a recurrence of the acute hemolytic exacerbations, and resulted in sustained rises in the hemoglobin, erythrocyte, and leukocyte levels. The importance of crises of abdominal pain as the chief presenting symptom of paroxysmal nocturnal hemoglobinuria is emphasized. It is suggested that the disease may be far commoner than is supposed. Attention should be directed particularly to diagnoses of "surgical abdomen" or atypical "refractory" anemia. While corticotropin certainly was of clinical value in the case reported, the wisdom and feasibility of its long-continued use may be questioned. The effect of the hormone on the underlying hemolytic process remains undetermined; the basic mechanisms of the disease must be determined.

Apresoline in Arteriosclerotic Hypertension.—Hydralazine (Apresoline) was administered to 17 elderly hypertensive arteriosclerotic patients for five to seven months in concentrations that caused a significant reduction of both systolic and diastolic pressures. Despite the large doses given (400 to 1,300 mg.), in only one patient was it necessary to discontinue the drug because of distressing side-effects. No cerebral or cardiac complications were noted. The mean value for cerebral blood flow increased after hydralazine and the cerebral vascular resistance decreased, suggesting a direct relaxing effect of the drug on cerebral vessels. The cerebral metabolic rate remained unchanged. While receiving hydralazine, many of the patients appeared to be clinically improved, and, on the substitution of placebos for hydralazine, deterioration became apparent. A marked improvement occurred in the manifestation attributed to cerebral insufficiency of 11 of the 14 hypertensive patients who were significantly improved. There is, however, no good correlation between the rate of cerebral blood flow and clinical status either before or after hydralazine therapy; this would seem to indicate that the observed mental improvement in mental status with hydralazine may not be directly related to hemodynamic changes.

American Journal of Ophthalmology, Chicago

36:1657-1790 (Dec.) 1953

Ocular Manifestations of Disturbances in Calcium Metabolism: Ninth Sanford R. Gifford Lecture. F. B. Walsh and R. G. Murray.—p. 1657.
Ocular Effects of Methyl Alcohol Poisoning: Report of Catastrophe Involving 320 Persons. C. D. Benton Jr. and F. P. Calhoun Jr. —p. 1677.
Therapeutic Value of Nebacetin in Ophthalmology. B. Lawaetz, H. U. Møller and G. Østerberg.—p. 1686.
Classification and Treatment of Allergies of Conjunctiva. F. H. Theodore. —p. 1689.
Electro-Encephalogram and Ocular Function. G. E. Park.—p. 1705.
Increased Intraocular Pressure Produced by Di-Isopropyl Fluorophosphate (DFP). T. N. Zekman and D. Snydacker.—p. 1709.
Ophthalmology in Korea. S. L. Jukofsky.—p. 1715.
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Retinoblastoma Treated with Intravenous Nitrogen Mustard. C. Kupfer. —p. 1721.
An Evaluation of Cyclogyl (Compound 75 GT). B. Milder and R. S. Riffenburgh.—p. 1724.

American Journal of Physical Medicine, Baltimore

32:331-410 (Dec.) 1953

Observations on Fatigue Patterns of Anterior Tibial Muscles. J. Wilder, T. C. Kenaston, P. A. Mabe Jr. and others.—p. 331.
Effects of Carbon Dioxide (20%) and Oxygen (80%) Inhalations on Movements and Muscular Hypertonus in Athetoids. T. Fay.—p. 338.
Some Eye Defects Seen in Cerebral Palsy, with Some Statistics. G. P. Guibor.—p. 342.
Some Problems for Psychological Research in Cerebral Palsy. N. Garmezy.—p. 348.

American Journal of Physiology, Washington

175:327-494 (Dec.) 1953. **Partial Index**

Effects of Adrenalectomy and Replacement Therapy on Brain Circulation, Oxygen Consumption and Electrocorticogram. J. R. Bergen, C. A. Hunt and H. Hoagland.—p. 327.
Hypercholesteremia in Hereditary Obese-Hyperglycemic Syndrome of Mice. J. Mayer and A. K. Jones.—p. 339.
Insulin and Relation Between Phosphate Transport and Glucose Metabolism. J. Sacks and F. M. Sinex.—p. 353.
Adaptation in Pressor-Receptor Reflex Mechanisms in Experimental Neurogenic Hypertension. W. G. Kubicek, F. J. Kottke, D. J. Laker and M. B. Visscher.—p. 380.
Hemodynamics of Carotid Sinus and Its Repercussion on Pressor Reflex. H. Mazzella and E. F. Migliaro.—p. 383.
Experimental Hypothermia: Respiratory and Blood pH Changes in Relation to Cardiac Function. J. J. Osborn.—p. 389.
Citrovorum Factor and Irradiation Injury. D. J. Buchanan, W. N. Pearson, C. Amarasingham and others.—p. 437.
Removal from Skin of Plasma Protein Labeled with Radioactive Iodine. R. P. Jepson, F. A. Simeone and B. M. Dobyns.—p. 443.
Validity of Bromsulphalein (BSP) Method for Estimating Hepatic Blood Flow. E. E. Selkurt.—p. 461.
Effect of Osmotic Gradients on Water Transport, Hydrogen Ion and Chloride Ion Production in Resting and Secreting Stomach. W. S. Rhem, H. Schlesinger and W. H. Dennis.—p 473.

American Journal of Public Health, New York

43:1501-1614 (Dec.) 1953. **Partial Index**

The Basic Unity of Private Practice and Public Health. H. R. Leavell. —p. 1501.
Status of Murine Typhus Infection in Domestic Rats in the United States, 1952, and Relation to Infestation by Oriental Rat Fleas. C. O. Mohr, N. E. Good and J. H. Schubert.—p. 1514.
Incidence of Tuberculin, Histoplasmin, and Blastomycin Reactors Among Group of School Children. M. L. Furcolow, J. Schwarz, B. A. Hewell and J. T. Grayston.—p. 1523.
*Detection and Occurrence of Coxsackie Viruses in Sewage. S. M. Kelly. —p. 1532.
Who Should Do What in Public Health? R. P. Kandle.—p. 1539.
Social Service in a Health Department. M. Grant.—p. 1545.
*Prevention of Trichinosis by Gamma Irradiation of Pork as a Public Health Measure. S. E. Gould, H. J. Gomberg and F. H. Bethell. —p. 1550.
Bactericidal and Fungicidal Effects of Ozone on Deliberately Contaminated 3-D Viewers. L. J. Warshaw.—p. 1558.
Field Studies on Two- and Three-Compartment Sink Manual Dishwashing. M. A. Shiffman.—p. 1563.

Detection of Coxsackie Viruses in Sewage.—Previous reports on Coxsackie virus recoveries from sewage gave rise to the following questions. How frequently do viruses occur in sewage and water during normal times? How well, if at all, do they survive standard water sanitation practices? Such information can best be obtained by the use of a simple, rapid, sensitive, and safe method for detecting viruses. The method described here consists of virus adsorption on, and elution from, ion-exchange resins. To sewage samples, 60 to 100 ml. of a 30% solution of bovine albumin was added to give a final albumin concentration of 0.5%. Dowex 1 resin (200 to 400 mesh, 10% cross linkage) was added to the sewage in the proportion of 10 gm. per 100 ml. of sewage and mixed for three to four minutes. The suspension was centrifuged at 2,500 rpm for 10 minutes and the supernate discarded. To the sedimented resin was added 1 or 2 ml. of 10% disodium phosphate, the phosphate and resin mixed for 5 to 10 minutes, and the mixture centrifuged at 3,000 rpm for 15 minutes. The eluate was drawn off, saved, and treated with antibiotics, 500 units of penicillin and 2.5 mg. of streptomycin per millimeter of eluate. These preparations were kept at 8 to 10 C. overnight before being injected intraperitoneally and subcutaneously into one-day-old and two-day-old mice. The development of limb paralysis or spasticity during a two week period was taken as presumptive evidence of the presence of Coxsackie virus. Confirmation was made by passage of brain or leg material from such mice into healthy suckling mice and by its failure to induce disease in older (10 to 12 gm.) mice inoculated intracerebrally. Microscopic examination for typical lesions was also carried out. Serologic identification was made by neutralization test with antisera from known strains of Coxsackie viruses. With this procedure, sewages were examined for Coxsackie virus content in relation to source, seasonal fluctuation, types isolated, survival during sewage treatment, and storage behavior. That resin adsorption improves the detection of Coxsackie viruses in sewage is clear because (1) virus was detected in resin-treated samples and not in the same samples untreated and (2) more virus was detected in resin-treated samples than in the same samples untreated shown to contain Coxsackie viruses.

Prevention of Trichinosis by Gamma Irradiation of Pork.—Gould and associates describe the life cycle of Trichinella spiralis and the symptomatology, treatment, and prognosis of trichinosis. They are concerned chiefly with various methods of control. During the past two years they conducted experiments on the effects of ionizing radiation on trichina larvae in vitro, in rat muscle, and in pork. When they exposed trichinous rat muscle to gamma radiation from cobalt 60, a dose of 15,000 r produced sterility of the larvae and a dose of 18,000 r inhibited maturation of the larvae. They also found that exposure of trichinous pork in commercial quantities to the action of similar doses of gamma radiation from waste fission nuclear material produces the same results, effectively preventing the disease in test animals fed irradiated trichinous pork. These doses produced no change in the flavor of pork. Furthermore, they do not induce any radioactivity in the meat, so that no injury is produced in any person who eats the meat. Calculations on the possible costs of irradiation of pork indicate that the cost per pound of pork would be 1.5 mills per pound or about 30 cents per hog. When atomic waste fission material becomes available for industrial purposes, it is expected that public health workers will cooperate with forward-looking pork processors in introducing this method for making pork safe for human consumption.

Angiology, Baltimore

4:457-544 (Dec.) 1953

Experimental Production of Ventricular Septal Defects. H. King, H. B. Shumacker Jr., N. Deniz and F. Vellios.—p. 457.
Circulatory Disorders. R. E. Funk.—p. 480.
Experimental Studies of Fate of Arterial Homografts. A. Bencini and P. Bellinazzo.—p. 483.
Prognostic Value of Electronic Oscillometer in Peripheral Arterial Diseases. S. S. Samuels.—p. 496.
Effect of Intravenously Administered Estrogen in Cardiovascular Disease. L. Gitman and I. J. Greenblatt.—p. 502.
*Anti-Hemorrhagic Action of *n*-Butanol in Advanced Cancer. E. Revici and R. A. Ravich.—p. 510.
Blood Vessel Bank—Its Possibilities. A. A. Lazzarini.—p. 516.
*Surgery of Coronary Heart Disease. G. Murray, J. Hilario, R. Porcheron and W. Roschlau.—p. 526.

Antihemorrhagic Action of *n*-Butanol in Cancer.—Six hundred patients with advanced inoperable and metastatic malignancies of all types were divided in two groups. In the first group of 256 patients, 18 (7%) had one or more episodes of profuse

bleeding; *n*-butyl alcohol (*n*-butanol) was not employed in any of these patients. Twelve (67%) of the 18 patients died as a result of hemorrhage despite the use of large doses of vitamins C and K. In the second group of 344 patients, 25 (7%) had one or more severe hemorrhagic episodes; *n*-butyl alcohol was employed as a routine measure for the control of these hemorrhages. In only one patient (4%) did *n*-butyl alcohol fail to completely control the bleeding for at least 24 hours. This failure occurred in a severely jaundiced patient in profound cholemia due to an obstructing cancer of the head of the pancreas. Ten illustrative cases are described in which hemorrhage was controlled with a saturated aqueous solution of *n*-butyl alcohol, administered intravenously, intramuscularly or orally, depending on the severity of the hemorrhage and the facilities available. In very severe hemorrhages, the intravenous route is most desirable since brisk bleeding can usually be stopped within two to three minutes; 5 to 10 cc. was the usual intravenous dose. A second injection was rarely necessary. Intramuscular injection may require 5 to 10 minutes to control bleeding, and, in cases in which bleeding has not ceased entirely by this time, a second injection may be needed. The intramuscular dose was also 5 to 10 cc. In some nonhospitalized patients, it was necessary to utilize the oral route of administration; one to two teaspoonsful in water every 10 to 15 minutes until bleeding stops was found effective. The saturated aqueous solution of *n*-butyl alcohol is nontoxic, nonirritating, stable, and self-sterilizing. The pharmacological mode of action of *n*-butyl alcohol is not entirely clear, but appears to be related to the effect exerted on the metabolism of abnormal tissues rather than on the clotting mechanism of the blood.

Surgery in Coronary Heart Disease.—Murray and co-workers carried out experiments in dogs in which, by perfusion of the distal segment of the coronary artery, successful repair of the artery proximal to this level could be obtained. By this means the infarct that is prone to occur if perfusion were not undertaken could be prevented. The most successful method of perfusion was accomplished by passing a small plastic tube through a branch of the divided internal mammary artery, subclavian or other artery, or a graft from one of these vessels, and having the tubing project through the end of the artery. With the coronary artery dissected out for a distance of about 1 cm., clips could be applied and within 30 seconds, by inserting the plastic tube in the distal segment of the coronary artery, the circulation could be restored. Three of 13 dogs survived with no infarction of the heart muscle. The animals were able to carry on normally with the coronary artery tied off, proximal to this anastomosis. Successful anastomosis was then easy to carry out between the end of the artery used (either the mammary or other branch from the aorta), and the involved coronary artery. One had a choice between an end-to-side of the coronary artery or, as an end-to-end to the distal segment of the coronary. Eight of 17 dogs survived and did well after the operation. There may be some possible application of this in man, as it is known that, in about 50% of fatal cases of coronary occlusion, the degenerative changes are localized to a short segment of vessel. If this area were defined by arteriography, there is the possibility of performing such an anastomosis successfully. This would sustain the heart permanently, or possibly, a thromboendarterectomy could be done later. The pathophysiology of the cause of death from coronary thrombosis was studied in experiments on the heart of animals; it was demonstrated that on ligation of the descending branch of the left coronary artery at a high level, the area of the heart about to be infarcted loses its contractibility, begins to dilate, and a large noncontractile bulge forms on the wall of the left ventricle that on systole of the ventricle dilates and causes a paradoxical systole. Concomitantly with this, the blood pressure falls and the cardiac output diminishes enormously. When, however, this bulging area is supported to diminish the size of this noncontractile cavity, the blood pressure is better maintained and the output improved. Further proof of the damaging effect of this expansion chamber was demonstrated by the improvement shown when this portion of the heart muscle was resected and the contractile muscle on one edge of the defect was sutured to the good contractile muscle on the other edge. The cardiac output improved immediately and the blood pressure rose. There is an advantage in using this procedure in coronary infarction, because, with the expansion chamber removed, the immediate disastrous effects that cause death are removed, namely, falling blood pressure with the remaining muscle unable to meet the demands to keep up the pressure. Moreover, the involved arteriosclerotic, stenosed, or thrombosed coronary vessel is also removed.

Annals of Allergy, Minneapolis

11:699-808 (Nov.-Dec.) 1953

Studies of Combined Action of Some Antihistaminic Agents. P. Naranjo and E. Banda de Naranjo.—p. 699.
Measurement of Gastric Acidity Following Oral Administration of Theophylline. S. H. Waxler.—p. 717.
Standardization and Antigenic Analysis of Pollen Extracts by Gel Diffusion: (An Abridgement). R. P. Wodehouse.—p. 720.
Allergy (By Sterols?). M. A. Solari, G. R. Moreno and M. N. G. de Fernandez.—p. 732.
*Parenteral Crystalline Khellin in Treatment of Chronic Bronchial Asthma: I. Clinical Evaluation. H. S. Tuft.—p. 740.
Emotional Aspects of Pediatric Allergy—Role of Mother-Child Relationship. A. J. Mitchell, L. Frost and J. R. Marx.—p. 744.
Intramuscular Phenergan: Preliminary Report. K. A. Baird.—p. 752.
Chemical and Pharmacological Characteristics of Antihistaminic Compound, Pyrrobutamine. M. H. Mothersill, J. Mills, H. M. Lee and others.—p. 754.
Metal Sensitivity in Eczema of Hands: Degree and Range of Sensitivity to Chromium and Its Compounds. L. E. Gaul.—p. 758.
Failure of Tyrosine-Niacinamide-Pyridoxine Mixture to Influence Allergic Disease. W. R. MacLaren, D. Goldstein and B. C. Eisenberg.—p. 763.
Hyposensitization by Combined Antigen-Chlor-Trimeton Injection. G. K. Spearman.—p. 769.
Evaluation of Natural Steroid Complex (Marisone) in Treatment of Allergic Disorders. S. Bloom and H. Markow.—p. 773.

Parenteral Administration of Khellin in Bronchial Asthma.—Khellin is known to possess vasodilator action on the coronary vessels, and some investigators gained the impression that this drug relaxes the smooth musculature in general, including that of the bronchus. Based on the bronchodilator action, the drug was used in asthma with generally favorable results. However, the side-effects of khellin presented a stumbling block in the treatment not only of angina but also of asthma. The studies described here were carried out to test the secondary effects of a khellin preparation suitable for intramuscular injection. The preparation is a suspension of crystalline khellin in sterile isotonic solution of sodium chloride, 1 cc. containing 50 mg. of the drug. Being a suspension, rapid absorption and action cannot be expected, instead, long-continued slow absorption, and consequent lengthening of any beneficial effect, should be anticipated. Some asthmatic patients present some wheezing during some part of every day. This type of patient is frequently resistant to both symptomatic and allergic management and may benefit most from a long-acting drug. A pilot study revealed that such patients experienced greater relief from the intramuscular injection of crystalline khellin suspension than other asthmatic persons. Injections were given to 45 patients at the rate of once or twice a week. The total number of injections for all patients was 296. Disregarding the 8 patients receiving only one injection, there remained 37 who could be followed sufficiently long to permit some conclusions. Control studies were made on three patients by substituting for the khellin suspension the same amount of buffered isotonic sodium chloride solution. Benefit was reported only when khellin was given. As a further control, a period of time was allowed to elapse, during which the asthmatic symptoms gradually returned. No permanent effect was noticed in any patient. However, the preparation differed from those previously used. In contrast to the severe local pain reported for other intramuscular preparations, the suspension caused only mild local pain in seven subjects. Gastrointestinal upset was reported by only one patient. As regard the symptoms of chronic asthma, appreciable degrees of benefit were obtained in 28 of 37 patients.

Annals of Internal Medicine, Lancaster, Pa.

39:1173-1384 (Dec.) 1953

Drug Induced Hypoplastic Anemias and Related Syndromes. E. E. Osgood.—p. 1173.
*Clinical Evaluation of Gitalin in Treatment of Congestive Heart Failure. S. P. Dimitroff, G. C. Griffith, M. C. Thorner and J. Walker.—p. 1189.
*Use of Angiocardiography in Selection of Patients for Mitral Valvular Surgery. H. F. Zinsser Jr. and J. Johnson.—p. 1200.
An Etiology of Scleroderma. I. Mufson.—p. 1219.
Fatal Transfusion Reactions from Contamination of Stored Blood by Cold Growing Bacteria. A. R. Stevens Jr., J. S. Legg, B. S. Henry and others.—p. 1228.
*Syndrome of Cough Syncope. A. Kerr Jr. and V. J. Derbes.—p. 1240.
Lymphocytic Leukemia: An Analysis of Frequency, Distribution and Mortality at the University of California Hospital, 1913-1947. M. B. Shimkin, E. L. Lucia, K. C. Oppermann and S. R. Mettier.—p. 1254.
Some Clinical Caprices of Multiple Myeloma: 15 Case Reports from Study of 75 Cases. S. O. Schwartz and M. Cataldo.—p. 1267.
Thrombocytopenia and Abnormal Bleeding in Multiple Myeloma. T. N. James, R. W. Monto and J. W. Rebuck.—p. 1281.
Failure of Hypertonic Saline in Treatment of Hyponatremia and Edema in Congestive Heart Failure. J. F. Uricchio and D. G. Calenda. —p. 1288.

Gitalin in Treatment of Congestive Heart Failure.—Amorphous gitalin, a cardiac glycoside isolated from Digitalis purpurea, was given a therapeutic trial in 35 men and 33 women between the ages of 20 and 90 years with congestive heart failure. The 68 patients were divided in three groups. Group 1 consisted of 15 patients who were digitalized with gitalin; most of them had never received any form of digitalis previously. Group 2 was comprised of 45 patients previously digitalized and satisfactorily maintained with other glycosides; these were transferred to maintenance doses of gitalin. Group 3 consisted of eight patients to whom digitalis leaf, digitoxin, or digoxin could not be given in effective amounts because of toxicity. In group 1, four patients were treated by a rapid method, the dose of the drug being 1 mg. given three, four, or six times per day until digitalization was attained. One patient required 1.5 mg. every four hours for four doses. The digitalizing dose varied from 4.5 to 8 mg.; the average dose was 6.5 mg. The remaining 11 patients of group 1 were treated by a slow method with 0.5 mg. of the drug given three or four times per day until digitalization was attained. The digitalizing dose varied from 5 to 8.5 mg. with an average of 7 mg. In groups 2 and 3 the maintenance dose was 0.5 mg. of gitalin daily. Gitalin was safely, comfortably, and effectively useful in initial digitalization, redigitalization, and maintenance digitalization of patients in heart failure. Detailed case reports were presented of the eight patients in group 3 in whom gitalin was of value in promptly and safely establishing digitalization and control of heart failure, while digitalis, digitoxin and digoxin were ineffective because of their toxicity. The clinical application of the wide difference between toxic and therapeutic dose in gitalin is an important advance in the pharmacology of cardiac glycosides.

Angiocardiography in Selection of Patients for Mitral Valvulotomy.—Of 150 patients with mitral disease studied by angiocardiography, 123 were operated on. There were 17 deaths, a mortality rate of 14%. Twenty-seven patients were not operated on; 16 of the 27 were rejected as surgical candidates after angiocardiographic study, while 11 were advised to undergo surgical intervention, but postponed or refused it. Six of the 11 have since died. Correlation of the angiocardiograms with the condition of the mitral valve as determined at operation or necropsy demonstrated two angiocardiographic findings to be characteristic of mitral stenosis: first, the sharp outline of the left atrium due to obviously greater opacification of the left atrium than the left ventricle; and second, the persistence of this differential opacification for abnormal periods of time. Of the 150 patients, 62 presented typical clinical findings of "pure" mitral stenosis. Sixty of these patients were operated on and were found to have mitral stenosis. In these patients angiocardiography showed the pattern characteristic for mitral stenosis, although it was modified to varying degrees in a few patients with left atrial clots. While angiocardiography readily confirmed the diagnosis in this group of patients, it may not be considered as an essential preoperative study, since clinical diagnostic error is unlikely and operation can be recommended justifiably on clinical grounds alone. The remaining 88 patients had prominent apical systolic murmurs and were suspected of having significant degrees of mitral insufficiency. Only 16 of these patients (18%) were rejected as candidates for surgery because their angiocardiograms were considered characteristic for "wide-open" mitral insufficiency. In the other 72 (82%) the angiocardiogram was considered characteristic of predominant mitral stenosis. Angiocardiography proved very helpful in the preoperative evaluation of this group of patients with loud apical systolic murmurs. Angiocardiography may establish the diagnosis of mitral valvular obstruction when the clinical findings make such a diagnosis difficult or uncertain; for example, in five patients, mitral stenosis was shown to be present when no diastolic murmur could be heard. The authors' experience indicates that patients with the characteristic angiocardiographic pattern of mitral stenosis have an excellent chance for surgical improvement despite the fact that auscultation may suggest the presence of predominant mitral insufficiency. Furthermore, significant improvement followed valvular surgery in five patients despite the initial estimate by the surgeon of an adequate valvular orifice together with a prominent regurgitant jet. The surgeon should be urged to widen such valves further if possible, when the preoperative angiocardiogram has indicated impairment of left ventricular diastolic filling.

Syndrome of Cough Syncope.—A syndrome of cough syncope, i. e., loss of consciousness preceded by coughing, is described in 40 robust, strong, large-chested, and slightly obese men between the ages of 25 and 65 years. Most classified themselves as heavy smokers. Alcohol was used liberally by all but four. Pulmonary diseases were associated with cough syncope in 30 of the 40 patients; 12 had pulmonary emphysema and 10 asthma. The cough was dry, unproductive in nature, often a cascading paroxysm accompanied by extremely vigorous muscular efforts. The number of attacks varied; some patients had but one attack; others had as many as 20 or 30 per day. The attacks varied with the course of the underlying respiratory disease, and when this was self-limited or remediable they disappeared with its passing. Although the course of the disease is usually benign, death occurred in one patient. The mechanism of the syncope is unproved. Treatment for the most part is symptomatic.

Annals Otol., Rhin. and Laryngology, St. Louis

62:923-1238 (Dec.) 1953. **Partial Index**

*Studies on the Otic Labyrinth: VI. Anatomic Explanation for Hearing Dip at 4,096 Characteristic of Acoustic Trauma and Presbycusis. A. C. Hilding.—p. 950.
Hemifacial Spasm: Affection of Facial Nerve. M. C. O'Donnell.—p. 969.
Diagnosis and Early Treatment of Lesser Facial Fractures. G. Lowenthal. —p. 995.
Granular Cell Myoblastoma of Vocal Cord. T. A. Maguda and J. M. Young.—p. 1035.
Myxolipoma of Base of Tongue: Report of Case. J. R. Ausband, J. A. Harrill and E. E. Pautler.—p. 1039.
Surgical Repair of Perforated Ear Drum. H. P. House.—p. 1072.
Research Study of Effect of Autonomic Nervous System on Internal Ear. J. H. T. Rambo, D. Wolff and G. Freeman.—p. 1149.
Unrecognized Cholesteatosis in Children. P. E. Meltzer.—p. 1174.
Intravenous Procaine in Treatment of Ménière's Disease. E. P. Fowler Jr. —p. 1186.
*Inner Ear Pathology Following Maternal Rubella. J. R. Lindsay, D. G. Caruthers, W. G. Hemenway and S. Harrison.—p. 1201.

Hearing Dip at 4,096 in Acoustic Trauma and Presbycusis.—Hilding points out that nerve deafness first becomes manifest in the range around 4,000 to 6,000 cps. It makes no difference what frequency of sound causes acoustic trauma, the first and greatest damage is here. It has been pointed out that the eddies described by Békésy change directions at about this point and might depress and put tension on the basilar membrane here. Other explanations, such as the proximity of the first half of the basal turn to the middle ear or the entrance of the cochlear branch of the internal auditory artery have also been offered. With the 4,000 to 6,000 dip in mind, Hilding dissected and inspected the basal turn of five cochleas. There seems to be a point of greatest impact on the structures in the cochlear canal some 6 to 8 mm. from the beginning of the basal turn. This might explain that hearing loss both from presbycusis and acoustic trauma is great-

est at 4,000 to 6,000 cps. The force of impact in this area applied a thousand times a second over a period of decades, although only slightly greater than elsewhere in the cochlea, might serve to stretch and wear the marginal insertion most at this spot. Severe impulses (or shock waves), such as from blasts or extremely loud noise might serve to cause this same type of damage, as might the sound found in certain noisy occupations. The stapedius and tensor tympani muscles contract with noise in such a way as to protect the cochlea from excessive amplitudes. However, the reflex time for these muscles is about 10 milliseconds. Many a powerful thrust could enter the cochlea in these 10 milliseconds and cause damage at the point of impact.

Damage to Inner Ear Following Maternal Rubella.—The abnormalities commonly found in infants whose mothers had rubella during the first three months of gestation are congenital cataracts, patent ductus arteriosus and other cardiovascular defects, deaf-mutism, microcephaly, dental defects, and a general stunting of growth and development. The occurrence of deaf-mutism was first described in 1943 in Australia. Lindsay and associates point out that the high percentage of deaf-mutism found following the Australian epidemics is in contrast to the much lower percentage reported by Goodhill and the still lower figures of 2 or 3% reported by Ivstam from Sweden. Their own report is based on microscopic studies made on both inner ears from four infants exposed to maternal rubella in the early months of pregnancy. The semicircular canals and vestibular structures of one ear of a fifth infant have also been studied. Three of these infants had other abnormalities commonly found after maternal rubella. One infant was known to have severe bilateral deafness and the ears showed a bilateral sacculo-cochlear type of lesion. The midterm fetus showed a lack of differentiation of the organ of Corti and the tectorial membrane, which in the light of existing information, may have been within normal limits. The abnormalities in the saccule consisted of thickening and distortion of the wall and adhesions to the macula with corresponding areas of macular degeneration. In the cochlear duct the malformations of the tectorial membrane and Corti's organ were considered to be the explanation for the loss of function. The reduction in the extent of the stria vascularis has been interpreted as an indication of the direct effect of the rubella virus which in turn permitted a greater concentration of the virus irritant in the endolymph, resulting in injury to the developing structures within the cochlear duct and saccule.

Antibiotics & Chemotherapy, Washington, D. C.

3:1183-1294 (Dec.) 1953. **Partial Index**

*Tetracycline, New Antibiotic. L. E. Putnam, F. D. Hendricks and H. Welch.—p. 1183.
Historical Perspectives of Antibiotics: Past and Present. F. Marti-Ibanez. —p. 1187.
Laboratory and Clinical Findings in Patients Treated with Carbomycin. A. H. Kutscher, J. D. Piro, E. V. Zegarelli and others.—p. 1194.
Aureolic Acid, A New Antibiotic. W. E. Grundy, A. W. Goldstein, C. J. Rickher and others.—p. 1215.
Four Year Study of Bacterial Sensitivity to Five Antibiotics Using Standardized Paper-Disk Method. M. Kenney, P. M. Johnson and J. S. Tatz.—p. 1221.
Amphomycin, A New Antibiotic. B. Heinemann, M. A. Kaplan, R. D. Muir and I. R. Hooper.—p. 1239.
Preliminary Notes on Griseomycin, A New Antibiotic. P. J. Van Dijck, H. P. Van de Voorde and P. De Somer.—p. 1243.
Oxytetracycline-Polymyxin B Ointment in Skin Infections. B. Appel. —p. 1258.
Hygromycin: I. Preliminary Studies on Production and Biologic Activity of New Antibiotic. R. C. Pittenger, R. N. Wolfe, M. M. Hoehn and others.—p. 1268.
Streptogramin, A New Antibiotic. J. Charney, W. P. Fisher, C. Curran and others.—p. 1283.

Tetracycline, a New Antibiotic.—A derivative of chlortetracycline (Aureomycin) has been developed by removing the chlorine atom from the molecule. Tetracycline (Achromycin), the new compound, is more soluble than chlortetracycline and under the usual test conditions more stable than chlortetracycline or oxytetracycline (Terramycin). These three drugs are similar in their spectrums of antibacterial activity, and their pharmacological properties are also similar. Capsules and tablets were prepared from the same lot of tetracycline hydrochloride and were administered orally. Tablets were given to 111 and capsules to 106 subjects. Tablets were found to cause more minor side-reactions than the capsules. Four of 217 subjects exhibited what may have been an allergic response to the drug. It was necessary to withdraw the drug from two of these. Nausea, vomiting, and diarrhea occurred in 5.5% of 217 healthy men administered 2 gm. of tetracycline daily for three days. In 32 patients with miscellaneous infections, tetracycline appeared to be as efficacious as the other broad spectrum antibiotics.

Arch. Physical Med. & Rehabilitation, Chicago

34:733-778 (Dec.) 1954. **Partial Index**

Present Status of Ultrasonic Therapy. J. F. Lehmann.—p. 741.
*Intensive Exercise Program for Use in Knee Surgery and Pathology. C. D. Dawson.—p. 750.

Intensive Exercise Program for Knee Injuries.—Normal stresses and strains on the bony skeleton are an essential stimulus to osteoblastic activity, and factors that decrease these forces lead to disuse atrophy and osteoporosis. Within 24 hours after immobilization the bone matrix begins to lose its osteoblastic activity; within 72 hours the protein-calcium balance is disturbed; and in three weeks the overload of free-circulating calcium in the blood leads to kidney stones. The cartilaginous surface becomes softened and thinner in an immobilized joint and loses much of its absorptive function, so that hemorrhagic or synovial fluid collects in the joint. The cartilage loses its smoothness and becomes "sticky" and adherent. The joint becomes stiff and painful. Immediate exercises are essential for early restoration of an effective knee, regardless of the injury. The graduated system of exercises that Dawson outlines was developed by Robertson and Hawk. After surgery the leg is placed in extension without immobilization. No pillow is allowed under the knee, as this would nullify the effect of the quadriceps exercises. During the first three days after operation exercises consist of (1) quadriceps setting—to capacity—usually, first day, 15 to 25 hourly, second day, 35 hourly, and third day, 50 hourly; (2) leg raising one to three repetitions hourly, and (3) foot exercises—dorsal, plantar flexion, inversion, eversion, circumduction, dorsal flexion with toe grip, 12 repetitions hourly. On the fourth day the patient begins gradual weight bearing, and on this and the fifth day the quadriceps, leg raising, and foot exercises are continued. On the sixth day walking begins as well as mild flexion and extension, and on this and through the eighth day the aforementioned exercises are continued and gradually increased. After that through the 14th day the exercises are continued, and heavy resistance and hydrogymnastics are added. These exercises have been called "the 14 day treatment regimen." At the end of that time, many patients are ready for discharge from the hospital. All have learned by experience the place of regular resistance exercises, are familiar with the prescribed exercises and their dosage, and are encouraged to continue treatments at home indefinitely. The superior results of this treatment are demonstrated in terms of knee-joint function and of the shortening of the period of hospitalization.

Blood, New York

9:1-102 (Jan.) 1954

Mediterranean Anemia: Study of 32 Cases in Thailand. V. Minnich, S. Na-Nakorn, S. Chongchareonsuk and S. Kochaseni.—p. 1.
Electron Microscope Study of Sectioned Cells of Peripheral Blood and Bone Marrow. J. Kautz and Q. B. DeMarsh.—p. 24.
New Observations on Sickle Cells with Special Reference to Their Agglutinability. M. Bessis, M. Bricka, J. Breton-Gorius and J. Tabuis. —p. 39.
Hodgkin's Specific Cells in Bone Marrow Aspirations: Brief Review and Report of Two Cases. E. D. Bayrd, G. S. Paulson and M. M. Hargraves.—p. 46.
Life Span of Elliptocyte: Hereditary Elliptocytosis and Its Relationship to Other Familial Hemolytic Diseases. A. G. Motulsky, K. Singer, W. H. Crosby and V. Smith.—p. 57.
Intravascular Life Span of Transfused Leukocytes Tagged with Atabrine. L. P. White.—p. 73.
Effect of ACTH in Periodic (Cyclic) Neutropenia. B. H. Chaiken.—p. 83.

California Medicine, San Francisco

79:415-468 (Dec.) 1953

Unilateral Renal Disease and Hypertension. E. Burns.—p. 415.
Determining Serum Bicarbonate: Simple Syringe Titrator and Colorimeter. C. W. Boone and J. B. Field.—p. 420.
Suicide and Public Health. H. Bauer.—p. 422.
Controlled Technique for Vein Stripping. M. Gordon and R. D. Payne. —p. 425.
Removal of Stones from Low in Ureter: Report on an Improved Method. B. M. Palmer.—p. 428.
Autopsy Reports of Pulmonary Carcinoma: Survey in Los Angeles County Hospital for 1951. G. G. Hadley and W. K. Bullock.—p. 431.
Rupture of Gastrointestinal Tract: Dealing with Lesions Caused by Non-Penetrating Trauma. H. B. Kirtland Jr.—p. 434.
Entozyme® in Treatment of Psoriasis. A. E. Ingels.—p. 437.
Pseudomonas Aeruginosa Infections of Eye. W. H. Spencer.—p. 438.
Mandibular Herpes Zoster: With Report on Use of Cortisone in Case with Geniculate Ganglion Symptoms. I. M. Shevick..—p. 444.

Cancer Research, Chicago

138:821-916 (Dec.) 1953

Antigenic Properties of Methylcholanthrene-Induced Tumors in Mice of Strain of Origin. E. J. Foley.—p. 835.
Attempts to Isolate Active Agent in Cysticercus Fasciolaris. W. F. Dunning and M. R. Curtis.—p. 838.
Estimation of Antileukemic Potency of Antimetabolite Aminopterin, Administered Alone and in Combination with Citrovorum Factor or Folic Acid. A. Goldin, N. Mantel, S. W. Greenhouse and others. —p. 843.
Amino Acid Analysis of Serum Proteins in Multiple Myeloma. F. T. Grisolia and P. P. Cohen.—p. 851.
*Experimental Production of Carcinoma with Cigarette Tar. E. L. Wynder, E. A. Graham and A. B. Croninger.—p. 855.
Synergistic Inhibitory Action of A-Methopterin and Diaminopyrimidine upon Leukemia L 1210 in Mice. E. M. Nadel and J. Greenberg. —p. 865.
Studies on Transplantable Chicken Lymphoma (RPL-12): I. Pathological Changes Following Transplantation of Tumor. R. Love and G. R. Sharpless.—p. 869.
Increase in Host Specificity of Transplantable Spindle-Cell Tumor in Mice. L. C. Strong.—p. 876.
Time Study of Incorporation of Radiophosphorus into Nucleic Acids and Other Compounds of Transplanted Mouse Mammary Carcinoma. C. P. Barnum, R. A. Huseby and H. Vermund.—p. 880.
Disappearance of Natural Heteroagglutinins for Human Erythrocytes from Sera of Rats with Progressively Growing Tumors. A. E. Bogden and P. M. Aptekman.—p. 890.
Effect of 2-Acetylaminofluorene on Growth and Composition of Liver of Rat. H. R. Gutmann and J. H. Peters.—p. 895.

Production of Carcinoma with Cigarette Tar.—A cigarette tar condensate was obtained with a smoking machine that simulated human smoking habits. The resulting tar was dissolved in acetone and applied to the backs of CAF_1 mice in a dosage of 40 mg. of tar-acetone solution three times a week. Control mice were painted with acetone. Of 81 tarred mice, papillomas developed in 59%. The first lesion was noted in the 33rd week, and the mean time of appearance was 56 weeks. Of 81 tarred mice, histologically proved carcinomas developed in 44%. The first carcinoma was observed in the 42nd week, and the average time of appearance was 71 weeks. Of 62 mice alive at 12 months, cancer developed in 58%. Seventy-one weeks constitutes approximately half the life span of CAF_1 mice. This corresponds roughly with the fact already noted that in the human about 30 to 35 years of smoking, or approximately half the life span, are required for the production of bronchogenic carcinoma. One carcinoma was transplanted for 4 generations, and another was growing in the 13th generation at the time of this paper. Control mice painted with acetone alone showed no skin lesions. At the end of 20 months of painting, 53% were still living, compared to 9.8% in the group painted with tobacco tars. The group of mice painted with croton oil in addition to the tar, starting in the seventh month, cannot be properly evaluated because of a greater number of deaths occurring during the 12th and 14th months, although within the period of observation no acceleration of cancer formation was noted. The group of mice started with acetone and receiving croton oil beginning in the seventh month showed roughening and thickening of the epidermis, but no tumor formation was noted. In all CAF_1 mice painted with 0.3% solution of methylcholanthrene in acetone cancer developed within 4½ months. The first papilloma appeared during the sixth week, with average appearance during the seventh week. The first carcinoma was observed during the 12th week, with a mean time of appearance of 16 weeks. The results obtained with CAF_1 mice establish condensed cigarette tar as a carcinogen for mouse epidermis. These studies provide a tool to determine and isolate the possible carcinogenic agent or agents within tobacco tar. At present it is not known which fraction or fractions in tobacco tars are carcinogenic. Combined chemical and biological studies are now in progress to search for such agents. Such studies are important in view of the data relating smoking to various types of cancer.

J. Am. Geriatrics Society, Baltimore

1:813-886 (Dec.) 1953

Mechanisms Underlying Some Epigastric Symptoms. S. Wolf.—p. 813.
The Coronary Problem in Relation to Aging. R. L. Levy.—p. 821.

PANEL DISCUSSION: INSURANCE COMPANIES AND THE AGING POPULATION

Life Insurance. H. B. Brown.—p. 826.
Retirement Plans. P. V. Reinartz.—p. 828.
Disability Insurance. H. R. Leffingwell.—p. 830.
Hospitalization and the Aged. C. L. Reeder.—p. 833.
Cerebral Hemodynamics and Metabolism in Subjects Over 90 Years of Age. J. F. Fazekas, J. Kleh and L. Witkin.—p. 836.
Realistic Approach to Rehabilitation in Geriatrics. S. G. Feuer.—p. 840.
Pathology of Spontaneous Myxedema in the Aged. P. A. Bastenie. —p. 845.
Health and Happiness After 60. M. W. Thewlis.—p. 850.
Breast Disease in Older Patients. L. P. River, J. Silverstein and J. W. Tope.—p. 854.
Indications for, and Results of Gallbladder Surgery in Patients Over 65 Years of Age. B. E. Brush and F. Zeller Jr.—p. 863.
Improvement of Longevity in Elderly Patients with Fracture of Hip. R. Goldsmith, J. A. Sterling and L. H. Block.—p. 869.

Journal of Applied Physiology, Washington, D. C.

6:317-386 (Dec.) 1953

Relationship of Body Composition to Basal Metabolic Rate in Normal Man. R. J. Wedgwood, D. E. Bass, J. A. Klimas and others.—p. 317.
Comparative Effects of Different Formed Elements on Normal Human Blood Glycolysis. G. R. Bartlett and A. A. Marlow.—p. 335.
Human Salivary Buffering Rate Measured in Situ in Response to an Acid Stimulus Found in Some Common Beverages. R. H. Oster, L. M. Proutt, E. R. Shipley and others.—p. 348.
Sodium Concentration Deficit: Nomogram for Replacement. A. V. Wolf and M. E. McDowell.—p. 355.
Oxygen Toxicity. Effects of Oxygen Breathing at Increased Ambient Pressure upon pCO_2 of Subcutaneous Gas Depots in Men, Dogs, Rabbits and Cats. C. J. Lambertsen, M. W. Stroud 3rd, J. H. Ewing and C. Mack.—p. 358.
Response to Life Stress: Evaluation of Some Biochemical Indices. H. Persky.—p. 369.
*Effects of Vitamin A on Visual Threshold. J. C. Peskin.—p. 375.
Directional Sensitivity of Semicircular Canals Following Unilateral Labyrinthectomy in Man. J. I. Niven and A. Graybiel.—p. 379.

Effects of Vitamin A on Visual Threshold.—Persons vary considerably in visual thresholds; this has been demonstrated both in randomly sampled populations and in populations that were very similar in environmental conditions over considerable periods. Diet, age, and the physiological balance of the person play significant roles in establishing the visual threshold. It has been established that, during periods of famine and also in controlled dietary experiments, lack of vitamin A is associated with loss of visual sensitivity. The experiments described here were made on subjects who were chosen from a group who had been under nearly identical dietary conditions for several months prior to their selection. From a large group, who had been tested for threshold, 60 subjects were chosen whose thresholds, after several determinations for stability, fell within the normal and slightly elevated ranges of the threshold distribution. The subjects were divided into two groups. Twenty served as controls, and 40 received 50,000 I. U. of vitamin A concentrate in the form of two capsules daily. During the subsequent period the subjects returned at four to six day intervals for redetermination of threshold. The author states that administration of vitamin A to persons with normal visual thresholds had little effect on the majority of subjects. A small percentage of the population who fall within the normal range of threshold variation show increase in sensitivity when they are given supplements of vitamin A.

Journal of Comparative Neurology, Philadelphia

99:437-688 (Dec.) 1953. **Partial Index**

Relations of Brain Centers to Normal and Abnormal Eye Movements in Horizontal Plane. E. C. Crosby.—p. 437.
Capacity of Regenerating Axons to Bridge Long Gaps in Nerves. S. Sunderland.—p. 481.
Structure and Significance of Peripheral Extension of Autonomic Nervous System. H. A. Meyling.—p. 495.
Investigations on Nature of Peripheral Factors Influencing Process of Motor Nerve Regeneration. D. H. L. Evans.—p. 561.
Identity of Posterior Dorso-Central Nucleus of Panegrossi. R. Warwick. —p. 599.
Human Thalamus; Anatomical, Developmental and Pathological Study: I. Division of Human Adult Thalamus into Nuclei by Use of Cyto-Myelo-Architectonic Method. A. Dekaban.—p. 639.

Journal of Immunology, Baltimore

71:385-452 (Dec.) 1953

Growth Curve of Virus of Herpes Simplex in Rabbit Corneal Cells Grown in Tissue Culture with Parallel Observations on Development of Intranuclear Inclusion Body. T. F. McN. Scott, C. F. Burgoon, L. L. Coriell and H. Blank.—p. 385.
Quantitative Studies on Anaphylaxis, Deallergization, and Desensitization. R. Baserga and F. Bergamini.—p. 397.
Virus Neutralizing Antibodies in Pooled Human Serum. N. F. Stanley, D. C. Dorman and J. Ponsford.—p. 402.
Studies on Herpes Simplex Virus: V. Fate of Viable Herpes Simplex Virus Administered Intravenously to Man. P. Geller, V. R. Coleman and E. Jawetz.—p. 410.
Biological Properties and Variations of Reactions of Encephalitogenic Agent in Nervous Tissues. P. K. Olitsky and J. M. Lee.—p. 419.
Some Properties of Herpes Simplex Virus. K. Munk and W. W. Ackermann.—p. 426.
Multiplication of Coxsackie Virus in Adult Mice Exposed to Roentgen Radiation. F. S. Cheever.—p. 431.
Studies on Psittacosis-Lymphogranuloma Group: IV. Demonstration of Specific CF Antibodies Following Absorption of Serum. R. Pollikoff and M. M. Sigel.—p. 436.
Factors Influencing Effect of Hemagglutinating Viruses on Tumor Cell Suspensions. A. E. Moore and L. C. Diamond.—p 441.

Kansas Medical Society Journal, Topeka

54:545-584 (Dec.) 1953

Facts Learned from Maternal Mortality Survey with Emphasis on Obstetric Hemorrhage. F. R. Lock.—p. 545.
Diverticulitis and its Confusion with Carcinoma in Sigmoid Colon. S. L. VanderVelde.—p. 549.
*Dracunculosis. R. E. Speirs and A. H. Baum.—p. 553.

Dracunculosis.—It is generally believed that in the United States infestation with Dracunculus medinensis, or Guinea worm, is limited to patients who acquired their infestation outside of the United States, or to fur-bearing animals. After briefly describing the life cycle of Dracunculus medinensis, Speirs and Baum present the history of a woman who had never been out of the state and had no personal contact with anyone who had been in an area infected with Dracunculus. She lived for one year in a Kansas town where the local water was not potable, and all drinking water was brought in by railroad tank car. In June, 1947, she underwent drainage of an infected kidney, the postoperative diagnosis being pyonephrosis. Six weeks later nephrectomy of the left kidney was done. A small draining sinus remained in the surgical scar, and when she returned to the clinic in June, 1949, the sinus was excised. She was again hospitalized in September of the same year because the sinus failed to heal. In October, 1950, the dense, scarred tract was excised. The tract ended rather abruptly, although there was still some scar tissue in the retroperitoneal area. The renal area was explored for a residual stone, but none was found. After a few moments a white worm was seen to crawl out of the sinus tract. It measured 0.2 by 4 cm. This worm was identified as a Dracunculus medinensis. The incision was closed with no. 0 chromic surgical sutures. A small Penrose drain was inserted. The postoperative course was uneventful except for a low grade temperature elevation and moderate serous drainage until Nov. 7, 1950. The operative area has remained healed since that time. In July, 1953, the woman's general condition was good.

Louisiana State Medical Society Journal, New Orleans

105:455-506 (Dec.) 1953

Gastrointestinal Hemorrhage: Panel I. Esophagus, Stomach, and Duodenum. G. McHardy, J. E. Bechtold and D. C. Browne.—p. 455.
Diagnosis and Treatment of Common Low Back Disorders. W. R. Hamsa.—p. 461.
Diagnosis in Low Back Disorders. G. C. Battalora and O. L. Pollingue. —p. 468.
Differential Diagnosis of Osteoid Osteoma. M. Sherman.—p. 469.
Pitfalls in Postreduction Management of Fractures. N. J. Accardo. —p. 474.
Leg Length and Weight Bearing Interrelations. G. N. Ronstrom.—p. 476.
Femoral Embolism Following Internal Fixation of Hip. J. F. Nabos. —p. 483.
*Personal Experience in Use of Homogenous and Beef Bone Implants; Supplementary Report. S. R. Terhune and P. W. Shannon.—p. 485.

Homogenous and Beef Bone Implants.—In the course of the two years ending April 17, 1953, 130 bone implants were done on 123 patients. Refrigerated homogenous bone was exclusively employed in 90 and beef bone in 39. In one spinal fusion the authors used a homogenous "H" graft at the fourth to the fifth lumbar vertebrae and a beef "H" graft in the lumbosacral joint. The report covers homogenous bone in 91 and beef bone in 40 operations. Some of the procedures were supplementary additions to aid union of long bone osteotomy sites; others were employed for reinforcement to reverse nonunion after long bone fracture, shelf construction to supplement acetabular roofs following hip dislocation in poliomyelitis, consolidation of the talonavicular and naviculocuneiform joints of both feet in flat-foot sufferers, and there was a large number of spinal fusions. Roentgenograms were repeated on 85 of the 130 procedures 6 to 17 months postoperatively. These films included 58 homogenous and 27 beef bone implants. Thirty-four (59%) of the homogenous transplants resulted in unions, while 17 (29%) remained questionable and 7 (12%) represented definite nonunions. Twenty-two (81%) of the 27 beef bone implants united, while 3 (12%) remained questionable and 2 (7%) resulted in nonunion. Three homogenous and one of the beef bone implants became infected postoperatively. This rate is almost identical with the rate during the 27 months preceding the existence of the bone bank, when the authors had four infections after 131 autogenous transplants. It is increasingly obvious that beef bone implants are not accompanied by any greater incidence of infection. Since a longer follow-up of implanted bone unions for at least two or three years postoperatively is required for definite evaluation, the present report should be considered preliminary as far as beef bone is concerned and supplementary to previous reports in regard to homogenous bone implantations. The authors' opinion that autogenous transplants stand the best chance for survival remains unchanged, but homogenous transplants are practical and result in a comparable number of unions. Beef bone implantations may not be so good as autogenous transplants, but their use has been proved safe and valuable for stimulating bone union.

Michigan State Medical Society Journal, Lansing

52:1257-1414 (Dec.) 1953

Treatment and Prophylaxis of Streptococcal Infections for Prevention of Rheumatic Fever. H. B. Houser.—p. 1289.
Heart Disease in Mid-Life. W. B. Kountz.—p. 1293.
Effect of Cortisone on Size of Experimentally Produced Myocardial Infarcts: Further Studies. A. S. Johnson, R. A. Gerisch, F. W. Girton and others.—p. 1298.
Role of Physician in Employment of Cardiac Worker. E. M. Kline. —p. 1300.
*Surgery of Mitral and Aortic Stenosis. J. Johnson.—p. 1306.
*Effect of Hexamethonium on Normotensive Heart Failure: Possible Correlation Between Mechanism of Essential Hypertension and Normotensive Heart Failure. A. G. Wilson.—p. 1310.
Some Clues to Integrative Study of Hypertension. L. A. Cantow and R. J. Weil.—p. 1316.
*Dicumarol Therapy in Treatment of Status Angina and Impending Coronary Thrombosis. D. S. Smith and M. C. Kozonis.—p. 1320.

Surgery of Mitral and Aortic Stenosis.—Johnson first discusses the selection of patients for surgery on the mitral valve. It is relatively easy to decide to operate on a relatively young patient with "pure" mitral stenosis and severe symptoms, but the difficulty increases when one is forced to evaluate the effects of other complicating factors. Age is no contra-

indication to operation, but the risk of operation is greater in older patients. Patients with rheumatic activity should not be operated on. If "right heart failure" cannot be overcome on a medical regimen, operation is a desperate risk, but, since it offers the only hope for such patients, they are often willing to take the risk. Frequently they are greatly improved. The presence of a loud apical systolic murmur suggests predominant mitral insufficiency. Johnson found angiocardiography most helpful in assessing the relative severity of stenosis and insufficiency. Disease of other valves complicating mitral stenosis was formerly considered a contraindication to operation, but aortic stenosis can now be dealt with surgically at the same time. Pregnancy is not a contraindication to operation; however, unless failure appears to be a threat on a medical regimen, operation may be deferred until after delivery. In discussing the surgical technique, the author says that, if finger fracture cannot be accomplished, a knife must be used. This was the case in about one-third of the mitral valves operated on. There were six operative deaths in the last 100 patients with mitral stenosis operated on; 43 obtained excellent and 42 moderate improvement; 6 improved little if any. In the initial 25 operations, the results were not so good. Aortic stenosis cannot be dealt with in quite the same manner as mitral stenosis. The patient with an isolated aortic stenosis does not go into heart failure on the right side until fairly late. When such a patient becomes incapacitated by dyspnea on slight exertion, he should be operated on. When aortic stenosis coexists with mitral stenosis, it should be corrected at the same time. Seventeen patients were operated on for aortic stenosis. Four of these died; one died from ventricular fibrillation at the time of operation, two died from cerebral emboli, and one died on the second postoperative day. All three patients who died postoperatively had extremely calcified valves. The calcium broke free and went to the brain in two of these. Of the 13 patients who survived, one has been helped little, if any. The others have been moderately or greatly improved.

Effect of Hexamethonium on Normotensive Heart Failure.—Wilson believes that there may be an intimate and significant relationship between essential hypertension and congestive heart failure. His studies with hexamethonium are intended as a preliminary step in exploring this relationship. He feels that in both hypertensive arteriolar disease and congestive failure, there may be a common denominator of peripheral nature. Since hexamethonium drugs have been used to reduce peripheral resistance and lower blood pressure, it seemed reasonable that their use would relieve congestive failure, especially in a digitalized heart. He chose patients who were relatively normotensive, in congestive failure, who had been digitalized, and who had been taking meralluride (Mercuhydrin) or other mercurial diuretics regularly. The histories of nine patients are presented. Hexamethonium was very successful in relieving the symptoms of congestive left heart failure. It is as valuable as aminophylline in acute left heart failure and has the added advantage that it can be given subcutaneously. The author suggests that this relief is due to a release of peripheral resistance, and he relates essential hypertension and normotensive left ventricular failure to one etiological factor of general tissue demand. This is in contrast to accepting these two conditions as separate entities and to regarding hypertension as being due to more central mechanisms, e. g., renal, hormonal, etc. The author makes a plea that a center equipped with proper facilities continue these studies.

Bishydroxycoumarin (Dicumarol) Therapy in Status Angina and Impending Coronary Thrombosis.—Smith and Kozonis point out that the continuous use of bishydroxycoumarin (Dicumarol) over a period of years, to prevent recurrent coronary occlusion, has been shown feasible and relatively safe by Nichol and his group. Their own interest in employing bishydroxycoumarin in the treatment of status angina, refractory to accepted therapy, and in the prevention of coronary artery thrombosis was stimulated by Nichol's publication and experience with their first patient treated with long-range bishydroxycoumarin therapy. To date they have treated 30 cases of impending coronary thrombosis and status angina with bishydroxycoumarin for periods of three months to two years. Dramatic relief of anginal pain resulted from adequate therapy. Complications, chiefly hemorrhage, occurred in 10% of the patients. No patient with an adequate prothrombin level (20 to 30%) had a coronary thrombosis. Vague gastric symptoms resulted from long-continued administration of bishydroxycoumarin, but they did not necessitate discontinuing the drug. In three instances, where the cooperation of the patient was not complete, thromboses resulted. Relief of pain, particularly angina decubitus, was so marked that the authors had the impression that the drug has some definite vasodilating effect. The ability of every patient adequately treated to continue at work appears to indicate more efficient coronary circulation. The authors feel that preventive bishydroxycoumarin therapy has a proper place in the treatment of impending coronary thrombosis and status angina antecedent or subsequent to myocardial infarction.

Minnesota Medicine, St. Paul

36:1201-1310 (Dec.) 1953. **Partial Index**

SYMPOSIUM ON MARGINAL NEUROSES IN EVERYDAY PRACTICE

Orientation. N. Johnson.—p. 1225.
Patient Consults. F. J. Hirschboeck.—p. 1227.
Dynamics of Emotions. H. P. Rome.—p. 1232.
Facts and Fallacies in Therapy. N. Johnson.—p. 1234.
Social Security for Physicians. C. B. Drake.—p. 1238.
Becker County Blood Bank. C. W. Moberg.—p. 1241.
Inguinal Herniorrhaphy. W. G. Schaefer.—p. 1246.
Injection Therapy of Varicose Veins Using Sylnasol Foam. H. A. Alexander.—p. 1249.
An Acute Cervical Tumor in Mentally Deficient Child. H. H. Bruhl.—p. 1253.
*Mental Deficiency in Child Whose Mother was Given Electric Convulsive Therapy During Gestation: Case Report. J. Yamamoto, E. M. Hammes and E. M. Hammes Jr.—p. 1260.

Mental Deficiency in Child Whose Mother Received Electric Shock Treatment During Gestation.—The woman whose case is presented had lost her first child after a long illness. She had always been very sensitive and had had feelings of inferiority. During her second pregnancy she seemed very nervous and one day took seven or more grains of phenobarbital. The next day she had visual and auditory hallucinations. The general physical examination and the neurological examination showed nothing abnormal, except that the fundus of the uterus could be palpated 2 fingerbreadths below the umbilicus. Mentally the patient was bland but cooperative. Her emotional responses were silly, labile, and inappropriate. She spoke excessively and in a rambling manner and described various visual and auditory hallucinations. She had no insight into the nature of her condition. The diagnosis was that of a schizophrenic reaction. She was hospitalized, and 12 electroconvulsive treatments were given. Two months after the last treatment, she was dismissed after having made satisfactory progress. She was clear mentally. Her daughter was born three weeks after she had left the hospital. The child examined at the age of 32 months was mentally deficient, but the authors feel that this was probably not due to the shock treatments. It will be of interest, however, to note the incidence of mentally deficient children from mothers who have received electric convulsive therapy during pregnancy.

New England Journal of Medicine, Boston

249:1005-1044 (Dec. 17) 1953

Major Surgery in the Aged. T. J. Anglem and M. L. Bradford.—p. 1005.
Syndrome of Anemia, Dysphagia and Glossitis (Plummer-Vinson Syndrome). J. T. Howell and R. W. Monto.—p. 1009.
Peptic Ulcer. D. T. Monahan.—p. 1012.
An Evaluation of Influence of Dl-Methionine Treatment on Serum Lipids of Adult American Males. G. V. Mann, D. L. Farnsworth and F. J. Stare.—p. 1018.
Needle Biopsy of Liver: I. Its Use in Clinical and Investigative Medicine. N. Zamcheck and R. L. Sidman.—p. 1020.
*Death Following Angiocardiography: Report of Two Cases After Administration of Diodrast and Neo-Iopax, Respectively. E. G. Dimond and F. Gonlubol.—p. 1029.
Late Ulceration 20 Years After Implantation of Radon Seeds: Report of Case. J. G. Downing and D. W. Folan Jr.—p. 1031.

Two Deaths Following Angiocardiography.—The authors report two fatalities following angiocardiography. The first patient died immediately after the injection of 60 cc. of 70% iodopyracet (Diodrast). Autopsy demonstrated aberrant pul-

monary veins, patent foramen ovale, and stenosis of the mitral valve. The second patient died immediately after the injection of 27 cc. of 75% sodium iodomethamate (Neo-Iopax). Autopsy demonstrated primary proliferative pulmonary arterial and arteriolar sclerosis. These two fatalities, which occurred despite adequate safety measures, induced the authors to review with extreme care the need for any angiocardiographic study. Their experience in more than 300 catheterizations of the right side of the heart without serious complications, but with two deaths in approximately 100 angiocardiograms, convinced them that catheterization is the diagnostic procedure of choice. They appreciate that the two techniques are not fully interchangeable, but in most patients competent catheterization, done by experienced observers, can supply precise, definitive information that is not subject to the vagaries of interpretation associated with the shadows of dye. The advantages of angiocardiography are in the speed of the test; no complicated manipulation or protracted laboratory work is necessary. However, the risk to the patient's life that is brought into play the instant the dye is thrust into the blood stream must be justified by an imperative need for diagnostic information valuable in terms of the patient's welfare and must offset the risk to his life.

New Jersey Medical Society Journal, Trenton

50:535-584 (Dec.) 1953

Current Concepts of Rheumatic Fever Prevention. H. L. Drezner.—p. 538.
*Prophylactic Use of Antihistamine in Blood Transfusions. W. G. Bernhard, H. Grubin and M. V. Bryan.—p. 542.
Puerperal Rectal Surgery. S. Zager.—p. 546.
Electrocardiography: Its Value and Limitations. F. A. Marshall.—p. 550.
Use of Trilene in Obstetrics. J. S. Madara and B. H. Libien.—p. 553.
Typhoid Fever: Report of Two Cases in Suburban New Jersey. A. Abraham and E. Cummings.—p. 558.
Skin Eruptions of Pregnancy. E. M. Satulsky.—p. 560.
Use of Purified Non-Protein Bacterial Component, Piromen, in Allergic Conditions. S. Aronoff and A. Ghaemi.—p. 564.

Antihistamine in Transfusions.—The parenteral use of methapyridene hydrochloride (Histadyl) as prophylaxis against reactions was studied in 1,004 transfusions given between May 18, 1952, and Dec. 30, 1952, at St. Barnabas Hospital in Newark, N. J. The transfusions ranged from 500 to 7,000 ml. of blood per patient; a total of 1,237 pints was administered. The over-all incidence of reaction was 2.68%. There were no hemolytic reactions in this series; but there were 11 allergic, 14 pyrogenic, and 3 doubtful ones. The last three occurred in two patients, one of whom had hypertensive cardiorenal disease and the other chronic leukemia; the reaction occurring in the first patient was thought to be due to cardiac overloading. Methapyridene administered subcutaneously 15 to 20 minutes before a blood transfusion lowered the over-all incidence of reactions to about one-half the incidence in other series in which an antihistaminic was not used. There was no control group in this series because it was felt that to deprive any patient of the expected benefits of the antihistaminic would be unfair. The authors used 0.5 cc. as the dosage of methapyridene, but feel that this ought to be increased to at least 1 cc. (20 mg.) for the first 500 cc. of blood, with an additional 0.5 cc. for each subsequent 500 cc. of blood, in order to prevent reactions.

Oklahoma State Medical Assn. J., Oklahoma City

46:269-292 (Oct.) 1953

Evaluating Medical Testimony. J. T. Hieronymus.—p. 271.
Groin Hernia in Industry. F. L. Flack.—p. 273.
Relation of Private Physician to Industry. K. Davis.—p. 276.

46:293-326 (Nov.) 1953

Emotional Aspects of Diabetes Mellitus. P. C. Benton.—p. 295.
Rigid Wire Fixation of Fractures in the Hand. H. B. Shorbe and W. L. Waldrop.—p. 301.
Toxic Encephalopathy Occurring During Topical Treatment for Tinea Capitis. A. H. Ungerman and M. S. Ungerman.—p. 304.
Diagnosis and Treatment of Urinary Tract Infections in Children. D. D. Albers, J. N. Lysaught and E. H. Kalmon.—p. 308.

Plastic & Reconstructive Surgery, Baltimore

12:383-471 (Dec.) 1953

*Treatment of Keloids and Keloidal Scars. E. A. Kitlowski.—p. 383.
Further Observation in Cleft Lip Repair. K. M. Marcks, A. E. Trevaskis and A. daCosta.—p. 392.
Alloy Steel Sutures in Repair of Cleft Lip and Cleft Palate. O. P. Large.—p. 403.
New Approach to Treatment of Abdominal Muscular Agenesis. K. L. Stephenson.—p. 413.
Determination of Survival Time of Skin Homografts in Rat by Observation of Vascular Changes in the Graft. A. C. Taylor and J. W. Lehrfeld.—p. 423.
Dosage Phenomenon in Rat Skin Homografts. J. W. Lehrfeld and A. C. Taylor.—p. 432.
Studies on Acute Body Irradiation in Animals: I. Effect of Streptomycin Following Exposure to Thermal Burn and Irradiation. H. Baxter, J. A. Drummond, L. G. Stephens-Newsham and R. G. Randall.—p. 439.
Symmetrical Palmo-Plantar Keratodermia and Its Treatment by Plastic Surgery (Podoplantoneoplasty). J. A. Pupo and R. Farina.—p. 446.
Anti-Helix Reconstruction in Protruding Ear Operation. R. E. Straith.—p. 454.

Keloids and Keloidal Scars.—Differential diagnosis between a keloid and a keloidal or hypertrophic scar is essential for the proper treatment of either condition. This is achieved by massaging the lesion with heavy oil every day over a period of months. A keloidal scar will soften under this treatment, but a keloid will not, because it is a fibroma, usually of the fibrous tissue of the corium. A keloidal scar is contracted fibrous tissue that can be aggravated by the resulting contracture of the surrounding skin causing it to thicken and simulate keloid. The cause of keloid and the tendency to keloidal scar formation is unknown and is probably due to varying degrees of faulty metabolism. In grafting, keloid scar formation can be minimized by removal of excess granulations from the surface to be grafted. A keloid requires surgical excision, but it should not be removed completely. Enough should be left so that the fibrous tissue itself can be sutured; care should be taken not to traumatize normal skin. The correction of a keloidal scar can be accomplished by complete or gradual excision, shifting of neighboring tissue to relieve tension, or grafting with skin or flaps, depending on the situation.

Psychosomatic Medicine, New York

15:563-648 (Nov.-Dec.) 1953

PANEL DISCUSSION: PSYCHOPHYSIOLOGICAL PROPERTIES OF THE ADRENAL CORTEX; RECENT, UNPUBLISHED ADVANCES.
Introductory Remarks. S. G. Margolin.—p. 563.
General Concepts of Adrenocortical Function in Relation to Response to Stress. F. L. Engel.—p. 565.
Relation of Adrenocortical Activity and Adaptive Behavior. I. A. Mirsky, R. Miller and M. Stein.—p. 574.
Psychic Effects of ACTH and Cortisone. P. Goolker and J. Schein.—p. 589.
Psychological Responses to ACTH and Cortisone: Preliminary Theoretical Formulation. H. M. Fox and S. Gifford.—p. 614.

Stanford Medical Bulletin, San Francisco

11:203-290 (Nov.) 1953. **Partial Index**

Blood and Nerve Supply of Joints. E. Gardner.—p. 203.
Alkaline Phosphatase Formation Throughout Human Menstrual Cycle. H. G. Sturz.—p. 210.
Metabolic Observations on Chorio-Allantoic Membranes Infected with Virus. B. Brown and K. Odenheimer.—p. 218.
Antiviral Chemotherapy: VI. Parenteral and Other Effects of Flavonoids. W. C. Cutting, R. H. Dreisbach and F. Matsushima.—p. 227.
Effects of Antibiotics on Treatment of Appendicitis. R. Cohn, J. D. Relfe and J. Firpo.—p. 230.
Reduced Ototoxicity by Combined Streptomycin-Dihydrostreptomycin Treatment of Tuberculosis: Follow-Up Report. W. E. Heck, H. C. Hinshaw, W. J. Lynch and others.—p. 234.
*Evaluation of 6-Mercaptopurine in Treatment of Leukemia: Preliminary Report. B. E. Hall, M. D. Richards, F. M. Willett and others.—p. 237.
Reiter's Disease and Pleuropneumonia-Like Organisms: Report of Two Cases. R. W. Schaffarzick and E. A. Mankle.—p. 262.
Effect of Colchicine on Visible Alimentary Lipemia. W. E. Naugler and B. J. Brown.—p. 274.

Evaluation of 6-Mercaptopurine in Leukemia.—Compounds acting as antimetabolites in nucleic acid synthesis are being investigated for possible tumor inhibiting activity; 6-mercaptopurine is one of these. This report deals with preliminary observations on the effects of 6-mercaptopurine administered

orally to 11 patients with acute leukemia, 1 patient with chronic granulocytic leukemia, and 1 patient with acute lymphoblastic lymphosarcoma. The ages of the patients ranged from 15 to 78 years. Dosage schedules varied from 2.1 to 6.7 mg. per kilogram of body weight. The total quantity of drug required to induce partial or complete remission varied from 2,250 to 13,500 mg. A total dose of 6,900 mg. was administered to one patient with acute aleukemic leukemia, and resulted in the induction of complete clinical and hematological remission. Of the 11 patients with acute leukemia, 2 patients in the terminal state of the disease died 9 and 12 days respectively after institution of therapy. Two patients, still under active treatment, have not responded favorably; six patients showed varying degrees of clinical and hematological improvement, signifying partial remission; and one patient has been in an essentially complete clinical and hematological remission for six weeks. In two patients remission has been induced a second time by reinstitution of 6-mercaptopurine therapy. Clinical remission of six weeks' duration was observed in the patient with acute lymphoblastic lymphosarcoma, and clinical and hematological remission was obtained in the patient with chronic granulocytic leukemia. The authors conclude that the incidence of initial remission in adults with acute leukemia was considerably higher than that observed previously with folic acid antagonists or hormone therapy. They admit that the results in a larger series of patients observed over a longer period of time may not be as favorable.

Tennessee State Medical Assn. Journal, Nashville

46:399-444 (Nov.) 1953

*Use and Abuse of Injectables in Office Practice. W. W. Taylor.—p. 399.
Abuses in Use of Antibiotics. C. A. Hartung.—p. 403.
Recognition of Lesions of Optic Chiasm: Report of Cases. H. C. Smith.—p. 407.
Management of Patient with the Post-Phlebitic Leg. R. M. Landry.—p. 412.
Preoperative Evaluation from Medical Viewpoint. W. R. Miller.—p. 417.
Milkers' Nodules. S. C. Garrison Jr. and C. E. Adams.—p. 420.

Injections in Office Practice.—Many physicians have had the experience of having patients call and say they want to come to the office to receive a "penicillin shot" for a cold. In spite of advice that penicillin is not the treatment for the common cold, he informs the physician that he will go where he can obtain such a "shot." Such an attitude probably stems from the fact that products such as penicillin and certain hormones, when first available, were more effective parenterally than orally. If patients could observe some of the very severe sensitivity reactions to penicillin they would be less insistent that such a drug be given. A single penicillin injection may result in hospitalization for days or weeks, because of hypersensitivity reactions with resultant fever, eruptions, and arthralgias. If the patient is still less fortunate, anaphylactoid reactions may occur, and death has resulted from such reactions. The author mentions other antibiotics that may cause annoying reactions. The injection of hormones is also frequently abused. Estrogen therapy for the climacteric in women should be reserved for palliation of severe vasomotor and psychosomatic disturbances. Such therapy is not essential for all women. Injections of vitamins are also frequently demanded by patients, although with a normal gastrointestinal tract, vitamins administered orally are just as efficacious as when given parenterally. Some vitamins, such as impure preparations of vitamin B, given intravenously have caused distressing symptoms, such as dyspnea, precordial distress, nausea and a sudden fall of blood pressure. Mercurial diuretics, however, preferably should be given parenterally either intramuscularly or intravenously, because although mercurial preparations for oral administration are available, they are much less effective. Many medications are just as effective and less dangerous if given orally than parenterally, and this should be impressed on patients.

Texas State Journal of Medicine, Fort Worth

49:847-910 (Dec.) 1953

Management of Cleft Lip Deformities. S. Glanz.—p. 850.
Lesions of Esophagus in Infants and Children. E. B. Singleton.—p. 855.
Peroral Endoscopy in Cardiac Surgery. W. H. Maloney.—p. 861.
Pulmonary Cysts. J. C. King and F. H. Cole.—p. 864.
Differential Diagnosis of Mild Painless Jaundice. J. C. Cain.—p. 873.
*Werner's Syndrome: Study of Adrenocortical and Hepatic Steroidal Metabolism. J. M. Bauer and J. W. Conn.—p. 882.

Werner's Syndrome: Adrenocortical and Hepatic Metabolism of Steroids.—Bauer and Conn mention Werner's first description of cataracts in connection with scleroderma in four siblings in 1904 and cite several American reports. The present communication deals with data obtained in the course of a metabolic balance study in a woman who had the typical signs of Werner's syndrome. Her height was only 4 ft. 8 in. (142.24 cm.). Graying of hair had commenced at 12 years of age. Deformities of toes, which first appeared at the age of 18, progressed to severe contractures with overlapping of some. Cataracts developed at the age of 28, and menses became irregular at 32. The voice became hoarse and squeaky at 35, and skin ulcerations appeared at 41. Axillary and pubic hair growth had always been scanty, and lately there had been thinning of the scalp hair. The patient's weight ranged between 68 and 83 lb. (30.8 and 37.6 kg.), and, whenever she gained weight it was distributed about the trunk. One of the patient's sisters had died at age 63 with an identical clinical picture. She was shorter than the patient, had gray hair at age 30 years and, cataracts at 45 years, and had scant body hair and a squeaky voice. Another sister had diabetes mellitus and cataracts. There was no evidence of illness similar to the patient's in the other five siblings or in the parents. Balance studies revealed normal metabolic and urinary steroidal responses to administration of corticotropin. However, in the absence of adrenocortical stimulation with exogenous corticotropin, excretion of 17-ketosteroids was subnormal, while excretion of formaldehydogenic steroid was elevated. Administration of compound S disclosed deficiency in hepatic conversion of this compound to excretory 17-ketosteroids, despite the absence of other indications of abnormal liver function. It is suggested that Werner's syndrome may consist primarily of an aberration in the hepatic metabolism of steroidal compounds.

Virginia Medical Monthly, Richmond

80:649-705 (Dec.) 1953

Radioactive Iodine in Treatment of Hyperthyroidism. K. R. Crispell, R. B. Gahagan and W. Parson.—p. 652.
Diagnosis and Treatment of Glycosuria. R. C. Green.—p. 658.
*Histoplasmosis of Larynx. C. T. Burton and P. A. Wallenborn.—p. 665.
Adenocarcinoma of Small Bowel. R. M. Hardaway III and B. H. Ostrow.—p. 669.

Histoplasmosis of the Larynx.—Histoplasmosis, a disease caused by the fungus Histoplasma capsulatum, is a relatively new medical entity. There is not much information on the disease as a whole, and less than 20 cases of histoplasmosis of the larynx have been reported. It is a disease that occurs in two forms—a benign, subclinical type not uncommon in certain areas and a disseminated or fulminating type that is rare. The former type has a good prognosis and the latter a poor one; the mortality in the disseminated type is high, and various attempts at treatment have been unencouraging. Successful treatment with ethyl vanillate of 5 out of 12 patients with progressive disseminated histoplasmosis has been reported by Christie. Propamidine (4:4′-diamidino 1:3-diphenoxy propane) may be of use in the treatment of histoplasmosis of the larynx. When extreme edema and granulomatous lesions are present in any chronic laryngeal condition, histoplasmosis should be considered as a possibility.

West Virginia Medical Journal, Charleston

49:339-372 (Dec.) 1953

Surgical Aspects of Chronic Pancreatitis. C. D. Hershey.—p. 339.
Problems in Tuberculosis Control in the Potomac Area. R. L. Smith.—p. 344.
Rene Theophile Hyacinthe Laennec. G. R. Maxwell.—p. 347.
Problems of Ageing Encountered in a Large Medical Care Program. H. J. Mayers.—p. 352.
Benign Strictures of Biliary Ducts: Report of Two Cases. L. B. Thrush.—p. 357.

FOREIGN

Archives Françaises de Pédiatrie, Paris

10:1013-1124 (No. 10) 1953

Electrophoretic Study of Serum Proteins in the Premature During the First Four Years of Life. R. Martin du Pan, J.-J. Scheidegger and H. Roulet.—p. 1013.

Dystrophy of Renal Origin in the Child. R. Jean.—p. 1026.

*Hibernation. A New Therapy in Infantile Pathology. Study of 49 Cases. P. Chédid, A. Fargeallah and M. Tabet.—p. 1051.

Hibernation, A New Therapy for Children.—Hyperthermia, which favors the growth of micro-organisms and disturbs the neurovegetative system, also has a destructive effect on the circulatory system and the musculature. Sometimes it appears without any obvious cause as an acute attack of fever accompanied by pallor; sometimes there is an indeterminate infection with a dramatic and feverish onset, as in toxicosis or infectious diseases, but whatever its origin the hyperthermic syndrome, which jeopardizes the homeostatic balance, is dangerous and prostrating and may result in death. Hibernation successfully arrests the effects of aggression in such cases and restores a condition of well-being in spite of the indifference and passivity it induces. It reestablishes homeostasis and limits metabolic disturbances, but it does not take the place of adequate general therapy. The etiological agent responsible for the hyperthermia must be determined, if possible, and active therapeutic measures, such as the use of antibiotics, transfusions, hydration, and oxygen, should be instituted. Careful surveillance, especially at the moment of reawakening, is indispensable. Trials of the method at Beyrouth in August, 1952, when the weather was excessively hot and many children were dying in a syndrome of pallor and hyperthermia, showed that artificial hibernation is the treatment of choice for hyperthermic conditions, whatever their cause. It is comparatively easy to apply, and any danger accompanying it is clearly less than that inherent in hyperthermia and its sequelae. The ganglion-blocking agents used and the doses given should vary with the requirements of each patient. Two groups of children were treated; the first consisted of 32 infants ranging in age from 1 month to 2 years, while the second contained 17, including one with bronchopneumonia who was only 7 days old. Hyperthermia was associated in several cases with various forms of toxicosis, bronchopneumonia, cerebrospinal meningitis, or athrepsia. There were 18 deaths, almost all of which were due to the initial gravity of the patient's condition. Hibernation should be started as soon as the syndrome of malignant hyperthermia is noted, because the results obtained depend on the promptness with which it is applied. Most of the children treated in this first series were in a preagonal state when it was instituted.

British Medical Journal, London

1:1-54 (Jan. 2) 1954. **Partial Index**

*Cortisone and A.C.T.H. in Treatment of Non-Rheumatic Conditions. G. M. Aber, G. N. Chandler and S. J. Hartfall.—p. 1.

Developmental Dysarthria. M. Morley, D. Court and H. Miller.—p. 8.

Estimation of Intrinsic Factor of Castle by Use of Radioactive Vitamin B_{12}. S. T. Callender, A. Turnbull and G. Wakisaka.—p. 10.

*Researches in Aetiology of Non-Specific Urethritis. R. R. Willcox.—p. 13.

Cortisone in Nonrheumatic Conditions.—Since cortisone and corticotropin (ACTH) became available in Great Britain in 1951, 78 patients have been treated with them at the General Infirmary at Leeds. Forty-three of these patients had nonrheumatic conditions; the effects of the two drugs in these patients is studied. Fourteen patients with disorders of the blood were seen. A favorable response occurred in three children with acute acquired hemolytic anemia, and in thrombocytopenic purpura apparent clinical benefit resulted in the two patients treated. No effects were produced in aplastic anemia, though one patient with acute agranulocytosis from thiouracil made a good response. The effect of corticotropin in leukemia was at best temporary. This small experience suggests that, apart from acquired hemolytic anemia and some cases of purpura, cortisone and corticotropin have little place in the treatment of blood disorders. Sixteen patients with disorders of endocrine function have been studied. Of nine patients with exophthalmic ophthalmoplegia only three responded well; the best results were obtained with corticotropin in cases of recent onset or rapid progression. Three patients with Simmond's disease have made a dramatic and sustained improvement while receiving corticotropin. Two patients showing the virilizing effects of adrenal hyperplasia have been treated by adrenalectomy and cortisone; in neither did the results appear to justify the risks involved. Seventeen-ketosteroid excretion was controlled in two pseudohermaphrodites by the use of cortisone. The beneficial effect of cortisone and corticotropin in asthma has been confirmed. The use of corticotropin by intravenous drip and of cortisone by inhalation usually brought prompt improvement. In two patients with nephrosis a considerable diuresis accompanied treatment, and in one of them the remission lasted more than a year. There is no evidence that corticotropin influences portal hypertension accompanying cirrhosis, though apparent clinical benefit occurred in one patient.

Nonspecific Urethritis.—In the clinics of England and Wales in 1951 there were 10,794 cases of nonspecific urethritis as compared with 14,975 cases of male gonorrhea. Nonspecific urethritis was apparently more frequently contracted from regular consorts than was gonorrhea, indicating a possible nonvenereal bias in its etiology. In the group with nonspecific urethritis, more patients were married, they tended to be older, and they were more likely to have achieved "white-collar" status than those with gonorrhea. There was no evidence to suggest that the practice of buccal or anal coitus was commonly responsible for the transmission of the urethritis. The disease tended to have a longer incubation period than gonorrhea. A study of 301 urethral cultures taken from patients with nonspecific urethritis before and after treatment and from controls suggested that the so-called "bacterial urethritis" was uncommon. The results of 412 complement fixation tests for lymphogranuloma venereum and 323 complement fixation tests for enzootic abortion in ewes showed nothing distinctive between serum from patients with nonspecific urethritis and from controls. A study of 234 skin tests for lymphogranuloma venereum, psittacosis, and cat scratch fever, on the other hand, showed more positive readings in the urethritis cases than in controls. From the examination of 1,463 Giemsa-stained urethral scrapings, it was considered that the bodies seen were products of inflammation and unconnected with the virus of nonspecific urethritis. Thus, if the inclusion bodies sometimes seen in these scrapings are responsible for the isolated case, the causative organism cannot be seen in the majority. Attempts to passage the virus into the lungs and brains of mice, guinea pigs, and conjunctiva, knee joints, and urethra of baboons were also unsuccessful. The virus of nonspecific urethritis has not been isolated.

Canadian Medical Association Journal, Montreal

69:567-672 (Dec.) 1953

Recent Advances in Thoracic Surgery. E. C. Janes.—p. 567.

Fatigue: Its Clinical Significance. W. B. Spaulding.—p. 570.

Lithosperm-Like Action of Certain Quinones and Related Compounds. R. L. Noble and R. C. B. Graham.—p. 576.

Adrenalectomy in Prostatic Cancer and Malignant Hypertension. C. D. Creevy.—p. 581.

Clinical Survey of Alcoholics. L. J. le Vann.—p. 584.

*Surgical Treatment of Mitral Stenosis. W. G. Bigelow, W. F. Greenwood, A. D. McKelvey and J. K. Wilson.—p. 588.

Anaesthesia for Emergency Surgery. A. B. Noble.—p. 597.

The Ataxic Child. J. K. Martin.—p. 601.

Acute Gaseous Cholecystitis. E. A. Ryan, E. Harrigan and S. F. Penny.—p. 606.

Cancer of Stomach: Survey of 411 Consecutive Cases. A. J. S. Bryant, C. H. Crosby, A. E. Perry and I. W. Bean.—p. 610.

Mental Illness Among Displaced Persons. G. C. Sisler.—p. 614.

Prolonged Labour. H. G. Smith.—p. 617.

Clotting Mechanism in Angina Pectoris. H. Z. Pomeranz, T. Beatty and F. Stohlman.—p. 621.

*Christmas Disease: Variant of Haemophilia. R. L. MacMillan and K. W. G. Brown.—p. 623.

Mitral Stenosis.—The authors operated on 65 patients with mitral stenosis, and an analysis was made of the first 35 cases with a follow-up of from six months to three years. All patients had had a definite disability, usually progressive. This series included patients in the terminal stages of their disease who had been complete invalids for several years with constant

cyanosis at rest. There were 6 deaths in the 65 operations. With a follow-up extending to three years, there have been no deaths later than the seventh postoperative day. In the first 35 cases there were 4 deaths; in the remaining cases the patients have all been improved. There were no deaths in the group of "ideal" patients, recognized by the authors before operation. The characteristics of this ideal patient are (1) clinical proof of mitral stenosis, (2) definite disability due to pulmonary congestion, (3) absence of other important diseases of the heart, e. g., mitral regurgitation, aortic valvular disease, or active rheumatic myocarditis, and (4) absence of chronic right heart failure. A patient of this type may be expected to benefit from surgery. Many patients, of course, deviate from this ideal, and, in some, unfavorable features do not prevent them from having excellent results from surgery. The outcome cannot be estimated before the operation; it is not dependent on the age of the patient, for one may encounter a firm, immobile, or grossly calcified valve in any age group and in both the "ideal" and "less favorable" groups of patients. In many cases the degree of improvement is remarkable. The ultimate result correlates well with the functional efficiency of the valve as judged by the palpating finger after commissurotomy or finger fracture. It would appear that when the valve is opened it does not re-fuse to any appreciable degree. The production of significant mitral regurgitation has not been a problem of the operation.

Christmas Disease.—Christmas disease is a condition clinically indistinguishable from hemophilia but caused by the deficiency of a clotting factor that is different from antihemophilic globulin. The thromboplastin generation test is a simple and precise method of detecting deficiency of this factor. By means of this test, 14 patients considered to have hemophilia were studied; 4 were found to have Christmas disease. Hereditary transmission of Christmas disease is identical with the sex-linked transmission of hemophilia, but, as in hemophilia, cases may arise spontaneously. The differentiation of this condition from hemophilia is of particular importance in regard to treatment. Plasma, blood, and serum all contain Christmas factor and temporarily improve the clotting mechanism in patients with this disorder. Antihemophilic globulin preparations and dried serum are of no value.

Journal of Hygiene, London

51:427-577 (Dec.) 1953. Partial Index

•Study of Rheumatic Fever and Streptococcal Infection in Different Social Groups in Melbourne. M. C. Holmes and S. D. Rubbo.—p. 450.

Enumeration of Streptococcus Faecalis, with Particular Reference to Polluted Waters. L. A. Allen, M. A. F. Pierce and H. M. Smith. —p. 458.

Toxoplasma Infection at Different Ages, Studied by Skin-Test Method. T. Hedqvist.—p. 478.

Influenza Complement-Fixation. Simple Quantitative Micro-Method. G. Belyavin.—p. 492.

Evaluation of Methods of Applying Oil to Bedclothes and Practical Application of Selected Method. R. Leslie.—p. 502.

Conglutination Phenomenon: IX. Production of Immuno-Conglutinin in Rabbits. A. M. Coombs and R. R. A. Coombs.—p. 509.

Measurement of Duration of Infection in Paratyphoid Fever. T. C. R. George, R. W. S. Harvey and S. Thomson.—p. 532.

Use of Culture Virus in Preparation of Foot-and-Mouth Disease Vaccine. W. M. Henderson and I. A. Galloway.—p. 546.

Rheumatic Fever and Streptococcic Infection in Different Social Groups.—Numerous studies have shown that serums of patients with rheumatic fever usually have an antibody titer (e. g. antistreptolysin O) that is indistinguishable from that of patients convalescent from streptococcic tonsillitis or scarlet fever, thus confirming the clinical observation that the onset of rheumatic fever is commonly preceded by an attack of tonsillitis. Epidemics of rheumatic fever have been reported after outbreaks of streptococcic infection in schools and in the Armed Forces. Trials of sulfonamide prophylaxis have shown that a reduction in the streptococcic infection rate is associated with a reduction in the incidence of recurrences in rheumatic patients. In the investigations described here, hospital records of 1,469 patients with rheumatic fever (including chorea) up to the age of 14 years were used to study the social distribution of the disease in Melbourne. On this evidence the incidence of rheumatic fever was three times greater in low than in high rental districts. The results of throat swab surveys and Dick tests on school children living in different districts showed that children in the poor districts contracted streptococcic infections more frequently than those in better districts. One factor associated with the carrier rate of Streptococcus pyogenes in the various social groups was the incidence of tonsillectomy. In the high rental districts where the tonsillectomy rate was high (60%) the Str. pyogenes carrier rate was 12.5%, whereas the rates in poor areas were 35 and 25.3% respectively. Differences in social incidence of rheumatic fever might, therefore, be explained by differences in social incidence of streptococcic infection, which, in turn, might be influenced by the incidence of tonsillectomy.

Journal of Tropical Medicine and Hygiene, London

56:277-302 (Dec.) 1953

African Histoplasmosis. G. H. V. Clarke, J. Walker and R. M. Winston. —p. 277.

Onyalai: Clinical and Laboratory Survey. S. M. Lewis and A. Luria. —p. 281.

Sensitivity of Cholera Vibrio to Antibiotics. M. A. Gohar.—p. 289.

Lancet, London

1:1-56 (Jan. 2) 1954

Benign Tumours of Lung. C. P. Thomas.—p. 1.

•Hexamethonium in Treatment of Hypertension. M. Harington and M. L. Rosenheim.—p. 7.

Sudden Death Following Injection of Procaine Penicillin. R. C. Bell. —p. 13.

Viscosity of a Test-Meal: Its Influence on Gastric Secretion and Emptying. J. N. Hunt.—p. 17.

Primidone (Mysoline) in Treatment of Clinical Petit Mal in Children. J. N. Briggs and J. Tucker.—p. 19.

Primidone in Treatment of Non-idiopathic Epilepsy. P. W. Nathan. —p. 21.

Pain After Haemorrhoidectomy: Use of Prolonged Wound Anaesthesia. M. Lee.—p. 22.

Safer Emergency Blood-Transfusion. R. A. Zeitlin.—p. 23.

Use of Polythene Catheters in Ureteric Transplantation. R. Dearing and S. Way.—p. 24.

Multiple Myelomatosis with Atypical Blood Changes. L. C. Manché. —p. 25.

Hexamethonium in Hypertension.—Harington and Rosenheim feel that after three years' use of hexamethonium an attempt could be made to define its role in the treatment of hypertension. They show that the subcutaneous route of administration is superior to the oral one, for various reasons, but even when hexamethonium is injected subcutaneously, undesirable symptoms attributable to its action are not entirely absent. Patients suitable for treatment with hypertension are those with malignant hypertension, hemorrhages or exudates in the fundi, evidence of left ventricular failure, or severe and incapacitating headaches. Renal disease is not a contraindication to treatment. Before the authors decide whether treatment with hexamethonium is indicated, they hospitalized the patient so that cardiac and renal function can be assessed and the response of blood pressure to rest and sedation can be observed. A test dose is administered (hexamethonium bromide, 25 mg. intravenously), and the reaction of the blood pressure to this dose is measured in both the lying and the standing positions. Sixty-two patients received test doses in this manner, and 26 of them were thought suitable for treatment. Treatment begins with a small dose, usually 25 mg. of hexamethonium bromide subcutaneously given three times daily. The dose is increased every few days until a level is reached at which there is a satisfactory fall in blood pressure. This level varied from 50 to 250 mg. for a single dose. After discharge from hospital, the patient returns for control of dosage at intervals of one month. Since October, 1950, routine treatment with hexamethonium has been started in 34 patients (including 7 who did not receive an intravenous test dose). Of these, 22 were treated for three months or longer and are further discussed. Fourteen of these patients had malignant hypertension. Rapid and sustained relief was obtained with hexamethonium in acute pulmonary edema and cerebral edema in hypertensive patients. Apparently the drug can produce a reversal from the malignant to the benign phase of hypertension.

Maandschrift voor Kindergeneeskunde, Leyden

21:389-424 (Dec.) 1953

Employment of Transverse Planigraphy in Children. G. C. F. Brinkbok, H. E. A. Fermin and E. J. Renaud.—p. 389.
*Megaloblastic Anemia and Vitamin B_{12}. T. D. Stahlie.—p. 396.
Acute Hemotogenic Osteomyelitis. H. W. Ten Cate.—p. 411.

Megaloblastic Anemia and Vitamin B_{12}.—Stahlie points out that macrocytic anemias with megaloblastic bone marrow are rare in infants. They differ from pernicious anemia by the absence of the typical degeneration of the posterior and lateral columns of the spinal cord and by the fact that they can be definitely cured without requiring continuous maintenance therapy. He describes the history of a girl of 5½ months who had been pale since birth but who otherwise had seemed well until six weeks before hospitalization, when she began to cough and to vomit mucus. A week before hospitalization the family physician had established that the hemoglobin level was 45% (Sahli), but after one week of iron therapy it was only 35% and so the child was hospitalized. Examinations revealed among others an erythrocyte count of 1,760,000. The infant was given a suitable formula and in addition ascorbic acid and vitamins E, A, and D, but during the first few days she ingested only an average of 575 cc. of her formula. On the fourth hospital day 5 mcg. of vitamin B_{12} was injected intramuscularly. On the day after that she took 850 cc. and thereafter continued to eat well. Sixteen hours after the injection of B_{12} the reticulocytes showed a decided increase, and after 40 hours the bone marrow showed improvement. Nine days later improvement seemed to have come to a standstill, and it was decided to give the same dose of vitamin B_{12}, but this time by mouth. This was again followed by increase in the hemoglobin content and in the erythrocyte count. The weight and general condition likewise improved, and the child recovered completely. Although the pathogenesis of the anemia was not clear in this case, an increased frequency of the disorder under poor economic conditions and during war suggested that nutritional deficiencies might be involved in some cases.

Medical Journal of Australia, Sydney

2:841-876 (Dec. 5) 1953

Virology as Independent Science. F. M. Burnet.—p. 841.
Some Remarks on "Compensation Inguinal Hernia." T. F. Rose.—p. 845.
Analeptic Effect of Succinate in Coma and in Confusional States. E. M. Trautner and E. R. Trethewie.—p. 848.
Mortality in Australia from Cancers of Respiratory System. H. O. Lancaster.—p. 855.

2:877-912 (Dec. 12) 1953

Further Observations on Epidemic of Aseptic Meningitis at Port Augusta. J. S. Covernton and J. A. R. Miles.—p. 877.
Use of Thermostatically Controlled Electric Heating Pads in Maternity Nursery. C. Isbister and J. Isbister.—p. 879.
Industrial Dermatology. I. M. Wartzki.—p. 882.
Lumbar Intervertebral Disk Lesion. A. R. Murray.—p. 884.

Minerva Medica, Turin

44:1457-1496 (Nov. 17) 1953. **Partial Index**

Latest Acquisitions on Treatment of Anemias. M. Baldini.—p. 1457.
*Block of Autonomic Nervous System in Six Patients with Delirium Tremens According to Technique Used in Artificial Hibernation. I. Sanguineti and R. Laricchia.—p. 1469.

Block of Autonomic Nervous System in Patients with Delirium Tremens.—The authors treated six patients with delirium tremens by blocking their autonomic nervous system according to the procedure that Laborit used in inducing hypothermia. After the patient was examined, intravenous infusion of 1,000 cc. of isotonic sodium chloride solution containing 5% dextrose was instituted. In the mean time 2 cc. of Largactil (10-[γ-diethylaminopropyl]-2-chlorophenothiazine hydrochloride), 2 cc. of Neoantergan, and 2 cc. of Mefedina were aspirated into a syringe. This mixture was then injected into the rubber tube of the perfusion apparatus in three 2 cc. doses at 30 minute intervals. This method of administration is safe because the autonomic nervous system is blocked gradually and the process may be easily interrupted if needed. When 500 cc. of the solution was left in the perfusion apparatus, two vials of vitamins of the B complex were added. Six hours after completion of the phleboclysis, an infusion was made into the subcutaneous tissue of isotonic sodium chloride solution containing 5% dextrose, a vial of hyaluronidase (Jalovis), and 1 gm. of ascorbic acid. Penicillin incorporated in a retarding medium was given in doses of 250,000 Oxford units every 12 hours to prevent bronchopulmonary complications. This procedure was repeated every 24 hours until the patient was improved. There were no side-effects in the authors' patients and the symptoms disappeared by the end of the second day of treatment. These medicaments were combined because Largactil acts centrally on the autonomic nervous system and has, in addition, a pronounced antiadrenalinic effect while Neoantergan has a marked vagolytic power and Mefedina a sedative effect. Because of their synergistic effect they can be given in relatively small doses thus minimizing the danger of the toxic effects of each of the drugs. The doses administered induced a deep and prolonged sleep, and on awakening the patient's temperature was reduced or normal, and the psychic and motor disturbances had subsided. The authors attribute this therapeutic effect not only to the sedative, hypnotic and antithermic action of the combination of the drugs but also to a hyporeactivity of all aggressive stimuli.

Münchener medizinische Wochenschrift, Munich

96:29-52 (Jan. 8) 1954. **Partial Index**

Clinical Contribution to "Functional Pathology." F. Hoff.—p. 29.
Unusual Forms of Renal Hypertension. R. Heintz, H. Losse and F. Görlitz.—p. 33.
Dietetic Treatment of Progressive Muscular Dystrophy (Erb). J. Evers. —p. 41.
*Bilateral Adrenalectomy in Patients with Inoperable Carcinoma of Mammary Glands. M. Saegesser.—p. 41.

Bilateral Adrenalectomy in Inoperable Mammary Cancer.—A regimen was devised whereby adrenal insufficiency was regularly prevented after surgical bilateral removal of the adrenal glands by substitution with cortisone in eight patients with inoperable mammary cancer. Substitution therapy was started two days before the surgical intervention. The first day 50 mg. of cortisone acetate was given twice, at noon and in the evening, and on the day before the operation 50 mg. of cortisone was given three times, in the morning, at noon, and in the evening. On the day of the operation 50 mg. of cortisone was given one hour before the operation, and this dose was repeated every six hours after the operation; on the first postoperative day 50 mg. of cortisone was given four times, every six hours. On the 2nd postoperative day 50 mg. of cortisone was given three times, on the 3rd postoperative day 25 mg. three times, on the 4th postoperative day 25 mg. two times, on the 5th and 6th postoperative day 25 mg. three times, and from the 7th to the 21st postoperative day 25 mg. daily. Desoxycorticosterone acetate (Percorten) in a dose of 5 mg. was given in addition to cortisone two hours before the operation, and in cases of low blood pressure after the operation 4 mg. was given to patients with a systolic pressure between 80 and 100 mm. Hg and 2 mg. to patients with a systolic pressure lower than 120 but higher than 100 mm. Hg. All the patients survived the surgical intervention without any manifestation of adrenal insufficiency. Beginning with the fourth postoperative week the daily maintenance dose of 25 mg. of cortisone may be reduced by 5 mg. if the patient is feeling well, and the dose may be reduced once more by 5 mg. after three to four days; however, 15 mg. is the limit that should not be exceeded. A simple and objective measure for the hormone dosage is the degree of pigmentation particularly beneath the eyes, which rapidly reacts in a positive or negative sense according to the hormone supply. The described regimen may be altered according to the individual patient; there may be patients in whom postoperative adrenal insufficiency may be compensated with considerably smaller doses of cortisone. It seems, however, advisable, to give too much than too little of the hormone since death from acute Addisonian crisis within the first 24 to 48 postoperative hours is unavoidable if the patient does not receive an adequate supply of cortisone in time.

Pediatria, Naples

61:849-1012 (Nov.-Dec.) 1953. **Partial Index**

Blood Picture in Patients with Tuberculous Meningitis Treated with Isoniazid. G. Ricci and T. Copaitich.—p. 849.
Electrophoretic Behavior of Hemoglobin in Mediterranean Anemia. II. Thalassemia Minor. F. Vecchio.—p. 863.
*Gamma Globulin in Prophylaxis Against Measles and Infectious Hepatitis in Children. V. Mione.—p. 901.

Gamma Globulin Against Measles and Infectious Hepatitis.—In November, 1950, a case of measles was reported at the University of Palermo pediatric clinic where children with tuberculosis were hospitalized. The infected child was from a ward occupied by 26 children of whom 6 had had the disease shortly before. He was isolated, and a single intramuscular injection of 2 cc. of gamma globulin was given to the others. Twenty-nine days later, a new case of measles developed; but the symptoms and skin eruption were mild and regressed within 24 hours. This one case was ascribed to an insufficient dose of gamma globulin. The spreading of the disease was prevented by the prophylactic treatment that in the other 24 children had produced passive immunity against the disease. Because 61 cases of infectious hepatitis (one fatal) had been reported during the same year at the same clinic, the author tried to obtain protection from this disease with the same method. Owing to financial limitation, the injection of gamma globulin could be given only to some of the children, and 178 with advanced tuberculosis and in very poor general condition were chosen. Nine days after the prophylactic treatment, the disease, with mild involvement of the liver and bilirubin in the urine, appeared in two of these children. Therapy was instituted and both recovered in 7 and 13 days respectively. The course of the disease was attenuated by the gamma globulin, which failed to prevent its onset probably because it was given too late after the time in which the two children had been exposed to the contagion. No other cases of the disease were reported for four and one-half months among these children. After this time it developed in another child and its course was severe. Therapy brought about recovery in 22 days. Twelve cases of infectious hepatitis occurred during the same four and one-half months in the 275 children who had not been given the prophylactic treatment. Thus a single injection of gamma globulin had produced a passive immunization against the disease that lasted four and one-half months.

Practitioner, London

171:591-694 (Dec.) 1953. **Partial Index**

Influenza. C. H. Stuart-Harris.—p. 595.
Upper Respiratory Infections in Infancy. A. P. Norman.—p. 601.
*Respiratory Infections in Old Age. R. E. Tunbridge.—p. 608.
Winter Aches and Pains. K. M. Robertson.—p. 613.
Chilblains. D. I. Williams.—p. 619.
Frost, Falls and Fractures. W. A. Law.—p. 625.
Pancreatitis, Acute and Relapsing. G. Blackburn and P. G. Large. —p. 641.
Treatment of Pernicious Anaemia and Allied Megaloblastic Anaemias. R. O. Gillhespy.—p. 648.

Respiratory Infections in Old Age.—Tunbridge shows that the difficulties of bacterial isolation and radiological examination in general practice, combined with the obvious limitations of some of the earlier anatomical classifications, justify a simpler classification of respiratory infection in the elderly into three groups: (1) infection of the upper respiratory tract, with or without spread to the lung, (2) respiratory infection with bronchospasm, and (3) respiratory infection associated with cardiac failure. The respiratory infection, with or without spread to the lungs, is potentially dangerous in the elderly, and the risk of spread to the lungs justifies bolder therapeutic measures than in the young adult. Respiratory infections associated with spasm often resemble an attack of asthma. Similarly, some forms of heart failure, particularly acute pulmonary congestion, delayed in onset after exertion or precipitated by infection may be indistinguishable from bronchitis associated with spasm. Finally, all too often congestive heart failure is, in the elderly, precipitated by a respiratory infection. So common is the association that special attention must be paid to the assessment and examination of the cardiovascular system in all elderly patients with a respiratory infection. Physical examination of the chest does not always settle the diagnostic problem. Dyspnea, tachycardia, cyanosis, and limited chest expansion may be observed in elderly patients with respiratory infection, with or without cardiac failure. In respiratory infection in the elderly, a complete diagnosis may be extremely difficult to reach during the first 48 hours. Therapeutic measures should be symptomatic, but also should aim at combating the infection, and should give careful attention to the cardiovascular system, the maintenance of the fluid balance, and the avoidance of anoxemia. Anoxemia is an indication for hospitalization.

Presse Médicale, Paris

61:1615-1638 (Dec. 9) 1953. **Partial Index**

*Discovery of a New Meningitis Caused by a Virus of Veterinary Origin (Epizootic Pseudoaphthous Stomatitis of the Bovidae). P. Mollaret, L. Salomon and Mme L. Salomon.—p. 1615.
Critical Study of Hypersplenism and Experimental Researches. G. Moretti, P. H. Castets and J. Kermarec.—p. 1620.
Fibrocystic Disease of the Pancreas. Its Surgical Aspects (Meconium Ileus). J. Bréhant.—p. 1627.

New Viral Meningitis of Veterinary Origin.—The ultravirus responsible for a new form of human meningitis has been traced to a disease affecting ruminants. The authors have given the disease the name of epizootic pseudoaphthous stomatitis of the Bovidae. The animal disease, which is akin to foot and mouth disease and the vesicular stomatitis of cattle, will be dealt with in a separate report. The clue to the etiology of the human disease lay in the fact that the four patients in whom it occurred were all workers at the Central Laboratory for Veterinary Research of the Ministry of Agriculture. The causative virus, isolated when various laboratory animals were inoculated with serum from one of the patients, was virulent even in concentrations of as little as 1:100. The stages in the development of the disease may be summarized as follows: (1) silent incubation for about seven days; (2) a first, generalized, illness, influenzal in character, accompanied perhaps by an enanthematous eruption; (3) three or four days of remission suggesting cure; (4) the appearance of acute meningitis with recurrence of the fever and general symptoms and an eruption of herpes, which constantly accompanied the onset of the meningeal signs; and (5) possible discrete relapses. Transient lymph node swellings were also noted during the meningeal phase of the disorder, and blood studies showed possible leukopenia with a decrease in the number of granulocytes. The patients in this series recovered, but their convalescence was prolonged: asthenia and trembling were persistent, and in three there was an abnormal increase of hunger. The clinical forms of this condition may be expected to vary according to the predominance of one or another of its phases; some may be merely febrile or pseudoinfluenzal, some may seem to be purely meningeal, and others may pass unnoticed.

61:1639-1666 (Dec. 12) 1953. **Partial Index**

*Hypophysectomy and Cancer of Breast. M. Perrault.—p. 1639.
*Indications for Segmental Resection in Pulmonary Tuberculosis: Study of 450 Operated Cases. E. Forster, C. Daniels and J.-M. Chamberlain. —p. 1641.
Intolerance to Sucrose in Children. P. Delthil.—p. 1643.

Hypophysectomy in Breast Cancer.—Perrault reviews the literature on hypophysectomy for carcinoma of the breast, a procedure that has been proved effective in experimental animals and tried to a small extent in human beings. He cites a case of his own in which the surgical intervention was well tolerated and a breast carcinoma, which had resisted all other forms of treatment, was stabilized. The patient had a slight bout of growth of a vertebral metastasis nine months after operation; she had been receiving a small dose of cortisone and thyroid extract for three months because of myxedema and amenorrhea caused by the hypophysectomy but untreated for the first six months postoperatively. The author feels that cortisone should not generally be used in such cases, since it is apt to reactivate a hypophyseal stump, if one remains. Subtotal exeresis of the hypophysis is considered adequate if it is 90%. The operation itself is not especially dangerous, but the poor results obtained in a certain series of patients treated by the

author and his associates have led them to set up two formal contraindications to surgery—functional respiratory disorders and intracranial hypertension. The author insists that hyperhormonal states of an inflational type ought to be treated immediately or, if possible, prevented because they constitute a background not only for endocrinogenital and psychosomatic disorders, but for a series of tissue reactions "which go in an uninterrupted chain from functional overstimulation to adenomas and cancers of the most rapidly evolving sort."

Indications for Segmental Resection of Lung.—The authors classify in five types the cases of pulmonary tuberculosis generally suitable for segmentectomy. These are the anatomoclinical forms of the disease considered to be indications of choice (tuberculomas and certain filled cavities), some cases from the 30% failure margin of thoracoplasty, cases in which proposed collapse therapy would probably be ineffective, urgent cases requiring effective and rapid treatment, and those cases in which cure by collapse therapy would entail an untoward loss of function. Other factors that must be taken into account in selecting patients for segmental resection are the clinical and radiological evidence, results from studies of respiratory function, and the social factors involved. Special indications for segmentectomy are homolateral cases in which it can complement a lobectomy and cases in which there are widely dispersed, heavily stratified lesions that do not permit collapse therapy. The mortality of this procedure was 3%, and a 93.7% cure was obtained in a series of 450 patients operated on, 50 in Strasbourg, France, and 400 in New York City and suburbs. Contraindications to surgery are respiratory insufficiency and extreme pathological infiltration. Even if these are not discovered until actual surgical intervention, they should still be respected; the surgeon must be prepared to give up resection in such cases, even after it has been started.

Schweizerische medizinische Wochenschrift, Basel

84:1-24 (Jan. 2) 1954

Physiopathology and Dietetics of Hypertension. H. Staub.—p. 1.
*More Recent Knowledge Concerning Hepatolenticular Syndrome. H. Hornbostel.—p. 7.
Concept of Tissue Therapy. R. Altschul and S. Fedor.—p. 11.
Prophylaxis of Phlebitis and Treatment of Varices in Course of Pregnancy. A. Hauser and K. Sigg.—p. 13.
World Research Program on Poliomyelitis. Communication of World Health Organization.—p. 14.
Friedrich Goll (1829-1903) and Tract of Spinal Cord Named After Him. H. Buess.—p. 15.

Hepatolenticular Syndrome.—Dimercaprol (BAL) was given a therapeutic trial in a 33-year-old woman and a 14-year-old girl with Wilson's hepatolenticular syndrome. The adult patient and an older brother had been exposed as gardeners to copper-containing insecticides; the older brother of this patient died in hepatic coma, and necropsy revealed cirrhosis of the liver and pseudosclerosis. The family history of the girl did not show that the disorder was familial. Aminoaciduria was present in both patients. Kayser-Fleischer's corneal ring also was observed in both and a sunflower cataract in the adult patient. Both patients had positive results from the sulfobromophthalein (Bromsulphalein) liver function test. Motor function was impaired and salivation was increased in both patients. The serum copper level was 79 mcg. per 100 cc. in the woman and 74 mcg. per 100 cc. in the girl. An excessive resting urinary output of copper was observed in both patients before the institution of the treatment with dimercaprol; a maximum value of 214 mcg. of copper per 100 cc. in 24 hours was determined in the girl. One intramuscular injection of 300 mg. of dimercaprol daily for seven days in the course of one month proved adequate for the mobilization of copper in the adult patient, but continued treatment with dimercaprol is required, since clinical improvement can be obtained only by continued copper elimination. The elimination of copper in the urine was considerably increased under treatment with dimercaprol; the maximum elimination values observed were 873 mcg. with 300 mg. of dimercaprol per day in the woman and 1,470 mcg. with 200 mg. of dimercaprol per day in the girl. In view of the concept that Wilson's syndrome is a disturbance of copper metabolism and the now afforded possibility of maintaining a continuous elimination of copper, determination of copper in the urine has gained in interest and significance concerning the diagnosis of the syndrome as well as the evaluation of the therapeutic effect of the drug employed. Serum copper values and aminoaciduria were not altered by the dimercaprol therapy. In contrast to observations by other workers, changes in the corneal ring of the patients were not observed by the author, but signs of regression of the sunflower cataract were observed in the woman. Continued treatment with dimercaprol for several months did not cause impairment or disturbance of the liver beside that revealed by the serum lability tests performed before the institution of the treatment. Salivation was reduced in both patients and the neurological symptoms were considerably improved. In the adult patient the handwriting test showed macrography before the treatment; handwriting was restored practically to normal during treatment. Results obtained with dimercaprol in these two patients confirmed the findings by Mandelbrote, Denny-Brown, and Porter that mobilization of copper can be obtained with dimercaprol in patients with Wilson's syndrome. The regression of the sunflower cataract in the adult patient provided evidence of the removal of copper from the organs that are considered as depots of copper. Urinary copper values and handwriting are important for the evaluation of the therapeutic effect of dimercaprol. The possibility is suggested that in hepatitis the copper metabolism also may be favorably influenced by dimercaprol in obtaining a more rapid regression of abnormal hepatic findings.

Semaine des Hôpitaux de Paris

29:4243-4324 (Dec. 30) 1953

*Clinical and Physiological Aspects of Phenylbutazone (Butazolidin): Role in Treatment of Rheumatic Conditions. G. Gaudin and W. Kuzell.—p. 4243.
*Brazilian Method of Antituberculous Vaccination by Large Doses of BCG Given Orally According to Arlindo de Assis. F. van Deinse.—p. 4248.

Phenylbutazone.—These observations on phenylbutazone are based on 409 patients with various rheumatic afflictions and other chronic conditions treated by the authors and 873 rheumatic patients reported in the literature. The drug was found to be especially effective in the treatment of acute forms of gout and periarthritis of the shoulder; it usually controls them in less than 48 hours. Phenylbutazone is also of value in inflammatory types of rheumatism. It appears to affect purine metabolism—this is an important aspect of its action that must be clarified. In the authors' experience, the toxicity of phenylbutazone has been less than that of butapyrine. The most frequent side-effects were edema and nausea. The drug possesses a potential toxicity on the granulocyte series of the elements of the blood, but the incidence of agranulocytosis was only 1%, and the condition usually yields promptly to cessation of medication and administration of corticotropin. A condition of agranulocytosis caused by a previous course of phenylbutazone therapy is not a contraindication to treatment, as long as the patient can be closely watched; also included in this category are well-compensated cardiopathy, minor hepatic insufficiency, and well-controlled renal insufficiency. Gastroduodenal ulcer, cutaneous hypersensitivity, and history of drug intolerance are the principal contraindications; concurrent radiotherapy should not be practiced.

Brazilian Method of BCG Vaccination.—BCG vaccination has been in use in Brazil since 1927, when some vaccinations were performed in Rio de Janeiro according to Calmette's method (three oral doses, each of 10 mg. of BCG in the first 10 days of life). This method and various modifications of it were used until 1950; in the meantime, Arlindo de Assis developed his method of concomitant vaccination, consisting in giving three successive doses of 30 mg. of BCG at birth and later five doses of 100 mg. a month apart. Sixty-one children living in contact with tuberculous persons were vaccinated by this method between February, 1945, and February, 1946, and followed up until February, 1950, at which time it was decided to extend the method to all children receiving vaccination. In approximately one-third of the children vaccinated by the concomitant method, the allergy to the

tuberculin tends to disappear. From 1947 to 1952 the mortality from tuberculosis in infants in close contact with tuberculous persons in one of Rio's worst slum communities was reduced to 0.84% by a revised concomitant method (100 mg. at birth and every month following until 600 mg. is reached). Among nonvaccinated infants in this community, the mortality was 3.13%. Since the administration of elevated doses of BCG has proved to be completely innocuous, indiscriminate administration without previous tuberculin tests is performed in São Paulo, with excellent results. The behavior of the allergy following one or more successive doses of 100 mg. of BCG vaccine was studied in children protected from all contact. After a single dose, the allergy does not always become positive, but the Mitsuda reaction to lepromin always does. Repetition of the doses of BCG can make tuberculin allergy disappear in children who had become allergic after the first 100 mg., and the Mitsuda reaction is reinforced by repeated doses of BCG. A vast campaign of vaccination by orally administered BCG vaccine has been in effect in the state of São Paulo since 1951; it is hoped that this will have a greatly inhibitory effect on both tuberculosis and leprosy.

Semana Médica, Buenos Aires

60:805-836 (Dec. 3) 1953. Partial Index

Late Results of Surgical Treatment of Sterility from Bilateral Tubal Obstruction: Fundamental Value of New Therapeutic Plan. J. F. Albertelli and C. D. Schiavo.—p. 805.
*ACTH Given Intravenously and Whole Fresh Blood in Treatment of Asthma: Preliminary Report. E. R. Sánchez.—p. 811.
*Prevention of Post-Transfusion Accidents: Experiences of 10 Years. J. E. Ottone.—p. 822.

Treatment of Bronchial Asthma.—The author observed in many patients with bronchial asthma that the results of corticotropin (ACTH) were transient and that administration of the drug was followed by aggravation of the symptoms on its discontinuation. He treated seven patients with acute bronchial asthma with intravenous injections of corticotropin combined with whole blood transfusion; 25 units of corticotropin were placed in 500 cc. of isotonic dextrose solution. Transfusion was made with 300 cc. of blood from donors of the opposite sex who did not have a history of allergic disease. Immediately after starting the transfusion, dipyrone (Novalgin) was given prophylactically. The corticotropin solution was given at a rate of 30 drops per minute, whereas transfusion was made at 60 drops per minute. When 250 cc. of the solution had been injected, 1 gm. of ascorbic acid in solution was added through the tube of the corticotropin solution, after which the procedure was continued. Blood transfusion was completed in 75 minutes, whereas the injection of the corticotropin solution took about four hours. The treatment was repeated three days later. Six patients were given this treatment twice and one patient three times. The symptoms of asthma disappeared a few hours after the first treatment in six patients and were greatly subdued in the patient who had the treatment three times. One year and a half after discontinuation of the treatment the symptoms had not reappeared in the former and were very mild in the latter. The author believes that the favorable results of the treatment were due to the fact that corticotropin, when in contact with blood, acquires the property of modifying the allergic terrain which is the cause of asthma. This article is a preliminary report.

Coramine in Prevention of Post-Transfusion Accidents.—When blood for transfusion is not combined with any of the well known antireactional drugs, the incidence of unpleasant post-transfusion reactions is about 5%, regardless of proper technique and care. In the course of the last 10 years the author observed that the addition of calcium gluconate or of the derivatives of pyrazole to the blood to be given diminishes the frequency and acuteness of the reactions, although it does not prevent their occurrence. In more than 300 blood transfusions the author prevented occurrence of the reactions by giving blood that contained 1.5 to 5 cc. of nikethamide (Coramine). Reports on the therapeutic value of nikethamide in controlling post-transfusion shock have recently appeared in the literature. It is added to the blood to be given. As an illustration the author reports four cases out of the large number he observed. Two patients had exchange transfusion in total quantities of 6 and 4 liters of blood, respectively. Every flask of 600 cc. of blood contained 1.5 cc. of nikethamide up to a total number of 10 and 7 flasks of blood respectively, containing 15 and 10 cc. of nikethamide, respectively. The drug at the aforementioned doses is harmless when contained in the blood. It is inexpensive and efficacious and is always at the reach of the physician.

Ugeskrift for Laeger, Copenhagen

115:1813-1854 (Dec. 3) 1953. Partial Index

*Results of Operative and Medicinal Treatment of Hyperthyroidism: Comparative Investigation. J. Piper and J. Rosen.—p. 1813.
*Treatment of Hyperthyroidism During Pregnancy. J. Piper and J. Rosen.—p. 1824.
Treatment of Skin Diseases with Hydrocortone: Preliminary Report. B. Heilesen, Å. Kristjansen and F. Reymann.—p. 1830.
Increase in Mortality from Cancer of Lung. E. Schiødt.—p. 1835.

Results of Operative and Drug Treatment of Hyperthyroidism: Comparative Investigation.—After studying the results of operative and medical treatment of hyperthyroidism reported in Danish hospitals, Piper and Rosen recommend operative treatment for patients with nodulous, retrosternal, or diffuse enlargement of the thyroid gland, for patients whose occupation or place of residence makes regular or long-continued control difficult, for patients without the ability to cooperate, which is essential in prolonged medical treatment, and for pregnant women. Medical treatment is advised for patients with severe complicating disorders involving high operative risk, some of whom may later become good subjects for operative treatment, and because of the risk of postoperative paralysis of the recurrent nerve, for teachers and singers. For the remaining and largest group, the choice is free. In the authors' opinion the treatment here should, in general, be medical as the mortality is about the same as with operative treatment, or slightly less. Irreversible side-effects are unknown except in the fatal cases, the period of inability to work is shorter, and, if patient or physician desires, the treatment with antithyroid substances can be terminated and surgical treatment resorted to later.

Treatment of Hyperthyroidism During Pregnancy.—Piper and Rosen studied 209 cases from the literature of hyperthyroidism complicated with pregnancy. The mild cases and those with pregnancy advanced more than five or six months were treated only with iodine, the grave cases, operatively after preliminary iodine treatment. One patient died in thyrotoxic crisis after cesarean section; none of the 122 patients treated with strumectomy died. The fetal mortality was about 9%. If pregnant women with hyperthyroidism are treated with antithyroid substances during the entire pregnancy, the frequency of recurrence is not higher than in nonpregnant women with hyperthyroidism, but the closer to the time of delivery the treatment is continued, the greater the danger of harmful effect on the fetus. If in order to lessen the danger to the fetus the duration of the treatment is reduced, the frequency of recurrence in the mother is greatly increased. In 13 of Piper and Rosen's 18 patients with pregnancy complicated by hyperthyroidism and treated with antithyroid preparations, they sought to reduce the danger to the fetus by discontinuing the treatment at least two or three months before the expected delivery. In the 16 ended pregnancies, 11 viable children were born, of whom 10 are normal; the 11th child, exposed especially long to the effect of antithyroid substances, showed retarded bone development and slight mental deficiency, but there was familial mental weakness. Recurrence after pregnancy appeared in 11 patients; over half of the recurrences are ascribed to interruption of the treatment for the sake of the fetus. Treatment with iodine and subtotal strumectomy is the preferred method for pregnant women with hyperthyroidism. With this treatment the danger in the combination of hyperthyroidism and pregnancy is so slight that there will rarely if ever be indication for interruption of pregnancy.

BOOK REVIEWS

An Atlas of Pelvic Operations. By Langdon Parsons, M.D., Professor of Gynecology, Boston University School of Medicine, Boston, and Howard Ulfelder, M.D., Assistant Clinical Professor of Gynaecology, Harvard Medical School, Boston. Cloth. $18. Pp. 231, with illustrations by Mildred B. Codding, A.B., M.A., Surgical Artist, Department of Surgery, Harvard Medical School. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; W. B. Saunders Company, Ltd., 7 Grape Street, Shaftesbury Ave., London, W.C.2, 1953.

This volume on the technique of operations on the female pelvis is divided into sections on abdominal operations, vaginal and perineal operations, and operations for malignant disease. The first section deals with pelvic operations performed through an abdominal incision and includes preliminary considerations, helpful hints for hysterectomy, modifications of total hysterectomy, conservative operations, operations on tube and ovary, operations involving the intestines and urinary tract, operations on the abdominal wall, and complications arising after abdominal operations. The second section discusses vaginal plastic procedures, combined abdominal and vaginal procedures, repair of fistulas, and minor operations. The third section describes Wertheim's hysterectomy with pelvic lymphadenectomy, combined abdominoperineal resection of the rectum, combined bilateral superficial groin dissection and radical vulvectomy, extraperitoneal iliac lymphadenectomy, vulvectomy, and radical groin dissection. The authors present the various techniques with which they are personally familiar. This avoids perpetuation in the literature of innumerable variants, some of which might have been described on the basis of limited experience and others of which have become obsolete or might have been tried and found wanting. For this reason the volume is authoritative and serves as a most reliable guide for those desiring information about the subjects in question. The simple, direct, and almost laconic descriptions of all the steps in the operations considered greatly enhances the readability of the text and permits those who are already experienced surgeons to acquire rapidly what they wish to know.

In the third section their modification of the Wertheim procedure with pelvic lymphadenectomy is quite radical, but, in contrast, the Miles operation for resection of the cancerous pelvic colon as described is rather conservative. Appropriate pelvic node dissection is not mentioned in connection with the latter, but, as the authors do mention, some combinations of the standard procedures they described may be improvised by the surgeon, and they have ably described pelvic and extraperitoneal lymph node excision. Exenterations are briefly discussed and due caution advised in their performance.

In a work as comprehensive as this one, certain omissions are bound to appear. For example, the reader is advised that he should have an excised uterus opened in the operating room lest he be surprised by a pathologist's report a day or two later that a small endometrial carcinoma, unsuspected clinically, was found. The authors do not comment on what, if anything, might be done in the event this is discovered in the excised uterus at operation. In the section on vaginal operations no mention is made of Schauta's radical vaginal procedure for cervical carcinoma, not even on expression of disapproval. No American text yet published includes this procedure despite adherents in other parts of the world. The authors ably describe intestinal surgery because intestinal structures are in the pelvis, and they deal with bladder and ureteral surgery for the same reason, yet in pelvic surgery the occasion does arise for nephrectomy, but this procedure through an abdominal incision is not described. Furthermore, omentectomy, either subtotal or total, is or should be part and parcel of certain situations in pelvic surgery, yet details of this procedure are not given. In any work on operative technique, the illustrations are of paramount importance. This volume is profusely illustrated by line drawings that are adequate although monotonous in style. The emphasis is placed on illustrating the surgical points and this principle has been uniformly adhered to. The type is large and permits rapid perusal without fatigue. The volume is so large that it requires considerable space on a table or flat top desk to open; it does not fit into a brief case, and the unusual width of the pages compared to their length does not permit easy handling for the reader who is reclining in a Morris chair.

The authors are to be commended for adding to the American literature a most valuable up-to-date work on pelvic operations. It may be consulted with great profit by students, interns, residents, general practitioners, general surgeons, urologists, and gynecologists. In this day of ever-narrowing specialization, bordering at times on the preposterous, this work should be an influence for rationality, especially in gynecology, for the surgeon who operates on the female pelvis must be proficient in handling any and all problems that may be encountered, not merely meeting those arising in one set of organs and ignoring structures a few centimeters away. For those responsible for training gynecologists, this work should serve as a guide to show them what the modern gynecologist should be trained to do.

Thoracic Surgery and Related Pathology. By Gustaf E. Lindskog, B.S., M.A., M D., William H. Carmalt Professor of Surgery, Yale University School of Medicine, New Haven, Conn., and Averill A. Liebow, B.S., M.D., Professor of Pathology, Yale University School of Medicine. Cloth. $15. Pp. 644, with 285 illustrations. Appleton-Century-Crofts, Inc., 35 West 32nd St., New York 1, 1953.

This book should be in the library of everyone interested in thoracic disease. It is excellently written, profusely illustrated, and considers thoracic lesions from the standpoint of fundamental disturbances as well as that of their practical clinical application. In addition to the authors listed, Drs. R. D. Alley, W. E. Bloomer, and F. C. Warring Jr. have contributed chapters. Particularly valuable because of their completeness are the chapters dealing with (1) surgical anatomy of the lung, in which the anatomy of the bronchial system and the vascular system are excellently illustrated by bronchovascular casts; (2) embryology and developmental abnormalities of the lung; (3) respiratory function and clinical evaluation; and (4) tuberculosis, which is discussed from the standpoint of pathology and medical and surgical treatment. Other chapters deal with mycotic infections of the lung; neoplasms of the lung; lesions of the thoracic-cardiovascular system, of the mediastinum, and of the diaphragm; preoperative preparation and operative and postoperative care of patients who have undergone thoracic surgery; and postoperative pulmonary complications. This book should be valuable to anyone interested in diseases of the thorax, whether he is a pathologist, internist, surgeon, or general practitioner.

Ulcers and Stomach Troubles: Their Causes and Relief. By Sidney A. Portis, M.D., Associate Clinical Professor of Medicine (Rush), University of Illinois Medical School, Chicago. Introduction by Morris Fishbein, M.D. Cloth. $2. Pp. 128, with illustrations. Hanover House, Garden City, New York; [Doubleday & Company, Inc., 575 Madison Ave., New York 22], 1953.

This interesting discussion of peptic ulcers is presented as a conversation between a doctor and his hypothetical patients. It will be of definite value to the author's patients, but, like all such books, it makes statements that other physicians might question. As in most medical books written for the laity, the difficulty of avoiding confusion in the mind of the patient is great and is not always overcome. The last chapter is an excellent résumé of the general principles of ulcer treatment and of the difficulties that arise during it. On the whole the book is interesting and useful, but neither it nor any other book can take the place of the conferences that the physician who treats peptic ulcer must have with his patients. Individualism in the treatment of peptic ulcer is the key to success.

These book reviews have been prepared by competent authorities but do not represent the opinions of any official bodies unless specifically so stated.

Saving Children from Delinquency. By D. H. Stott, Ph.D., Research Fellow, Institute of Education, University of Bristol, Bristol, England. Cloth. $4.75. Pp. 266. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1953.

This excellent treatise is an extension of the author's earlier report, entitled "Delinquency and Human Nature." Dr. Stott, a psychologist, believes that the psychologist must "give his work social relevance by making his findings available to the worker in the field." His aim was "not to be dogmatic about particular procedures so much as to inculcate a greater awareness of the field worker's function within a developing community—to relate, for example, the way in which a House Mother runs a particular Children's Home to our future as a nation." He shows that "beneath our contemporary crime statistics lies an inarticulate mass of mental suffering" and that "wrong doing springs from misery of an inner kind." The author sees the delinquent as an essentially unhappy person who is looking for a face-saving way to abandon his false bravado and shows that the attitudes of young persons are conditioned by the attitudes of others toward them. The primary emotional needs of human beings, whether young or old, are for affection and a feeling of counting for something. Among the chief causes of delinquency are the broken home and the lack of community cohesion in our large industrial cities. Any institutional environment is unsatisfactory from the viewpoint of personality development. There are interesting and informative chapters on grade schools and youth clubs.

The author's approach is neither overly optimistic nor overly pessimistic but realistic at all times. Although he firmly believes that we can not only save the child from delinquency but save some delinquents from further delinquency, he realizes this is no easy task. Stott shows that delinquency is not related to a low intelligence quotient and that, in fact, the very significance of a low IQ is open to serious doubt. There is a bibliography and an index. This volume is recommended for the teacher, social worker, family doctor, and all others who come in contact with potential delinquents.

The British Contribution to Medicine. By Dr. Jaime Jaramillo-Arango. Foreword by Sir Arthur MacNalty, K.C.B., M.D., F R.C.P. Cloth. $6. Pp. 220, with 45 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, 1953.

The author of this interesting book, originally a surgeon, spent the years during World War II first as minister, then as ambassador of Colombia to Great Britain. He believes that the great contributions to medical science have not been accidental as is sometimes alleged. Surely the discoverer must possess a keen awareness of the possible significance of the phenomena he observes, especially when they deviate from what is usual or expected. Among the scientists to whom the author pays tribute are William Harvey, discoverer of the circulation of the blood; Sir James Mackenzie, inventor of the polygraph; Sir Charles Bell, who first differentiated sensory and motor nerves; John Dalton, who described color blindness; Thomas Addison, who described pernicious anemia and hypoadrenalism; Thomas Hodgkin, who described pseudoleukemia; Sir William Osler, the great teacher and clinician; Sir Humphrey Davy, discoverer of the anesthetic properties of nitrous oxide; Michael Faraday, who, among other things, suggested the use of ether as an anesthetic; Sir William Leishman, who discovered Leishmania; Major Charles Donovan, who showed that kala-azar was a form of leishmaniasis; Sir David Bruce, discoverer of Brucella melitensis and of the trypanosome carried by the tsetse fly; Charles Best and Sir Frederick Banting, who discovered insulin; Sir Alexander Fleming, who discovered penicillin; Edward Jenner, the first man to use cowpox virus in the prevention of smallpox; Sir Ronald Ross, who showed that malaria was transmitted by mosquitoes; Sir Patrick Manson, who showed that filariasis was transmitted in the same way; and many others. Special chapters are devoted to salmonellosis, antibiotics, malaria, avitaminosis, and the struggle for cancer control. Most of the illustrations are portraits of those who have made outstanding contributions to medical science. The book has an index. It will delight all who have a special interest in medical history.

An Approach to General Practice. By R J. F. H. Pinsent, M.A., M.D. With foreword by Sir Lionel Whitby, C.V.O., M.C., Regius Professor of Physic, University of Cambridge, Cambridge, England. Cloth. $3.50. Pp. 166. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, 1953.

The author of this treatise on general practice is an active practitioner in Birmingham, England, who has spent much time in thinking about the day-by-day problems of general practice and the ideals to which doctors should aspire in their daily contacts with their patients. It is very readable, embellished by an engaging humor, and abounds with sound advice that might apply to practice in any community, even though portions of the book necessarily are pertinent only to the British Isles. The writer approaches the subject with a philosophy that should be valuable to anyone who intends to pursue this type of medical career. The book is full of practical suggestions in regard to setting up an office and the relationships between patient and doctor and between doctor and hospital. It is pointed out that the physician should actively ally himself with his colleagues in the community and, in cooperation with them, arrange his practice so that he may be free a definite time each week. The author emphasizes the necessity of keeping up with modern medical advances by taking full advantage of continuing education in the form of postgraduate instruction. There are excellent suggestions concerning the relationship of psychosomatic disorders to illnesses to be found in the general run of patients, with an awareness of the part played by environmental factors in disease. It is refreshing to find the author urging the use of all of one's faculties to attain a picture of the patient as a whole. The suggestion that it is the duty of the practitioner to educate his patients to be self-reliant is very timely. One gains the impression that Dr. Pinsent has lived a very full and satisfactory life in working out a successful medical career. Students, interns, and those interested in practice should profit by reading this excellent little monograph.

Salmonellae and Shigellae: Laboratory Diagnosis Correlated with Clinical Manifestations and Epidemiology. By Alfred J. Weil, M.D., and Ivan Saphra, M.D. Cloth. $7.75. Pp. 247, with 14 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., Toronto 2B, 1953.

The aim of this book is to make conveniently accessible the facts needed for handling the laboratory aspects of Salmonella and Shigella infections. Most of the text is devoted to a description of the methods used in the isolation and identification of these organisms. In addition, sections on their biology and the clinical and epidemiological aspects of the diseases caused by them are included.

Anyone who writes a book intended to be an up-to-date reference in a rapidly changing field runs the risk that it will be outdated by the time it is published. This seems to be the case here, particularly in the sections dealing with the Shigella group. Unfortunately, there are also errors and omissions that indicate incomplete coverage of the literature; for example, the nomenclature of the Shigella group is somewhat confusing because the classification of the Shigella Commission of the International Enterobacteriaceae Subcommittee was introduced after the original manuscript was written. In the sections on laboratory methods, several culture media used in the isolation of Salmonella and Shigella organisms are well discussed, but the failure to mention bismuth sulfite agar for the isolation of S. typhi is a serious omission. It is also unfortunate that brilliant green agar was not mentioned. The method of collecting specimens, which is so important in getting successful Shigella isolations, is unsatisfactorily presented. The relegation of the rectal swab to the position of being a good means of specimen collection only on mass examinations and the inaccurate description of the swab itself can be explained only by a lack of awareness by the authors of the utility of this simple laboratory tool. In the section on epidemiology of shigellosis the statements that milk is an important vehicle for Shigella organisms and that there is no direct proof of insects playing a role in the spread of shigellosis will be seriously doubted by workers in this field. The illustrations are excellent, with the exception of figure 7, in which a schematic representation of the reactions of Enterobacteri-

aceae on Kligler's iron and TSI agar are presented. The colors used are not representative, and the black color indicating formation of hydrogen sulfide is shown only as a small streak in the bottom of the tube, although actually most of the tube usually turns black. The inaccuracy of some of the information and the apparent inadequate coverage of the literature limits the usefulness of this book as a reference for the laboratory diagnosis of salmonellosis and shigellosis, even though it does contain much information on the biological and immunological properties of these organisms and the methods used for isolation and identification.

Vitamins and Hormones: Advances in Research and Applications. Volume XI. Edited by Robert S. Harris, Professor of Biochemistry of Nutrition, Massachusetts Institute of Technology, Cambridge, G. F. Marrian, Professor of Medical Chemistry, University of Edinburgh, Edinburgh, Scotland, and Kenneth V. Thimann, Professor of Plant Physiology, Harvard University, Cambridge, Massachusetts. Cloth. $8.50. Pp. 356, with illustrations. Academic Press, Inc., 125 East 23rd St., New York 10, 1953.

This publication presents a series of eight reviews by 13 contributors, dealing with current developments in basic science studies of certain vitamins and the hormones of the thyroid, adrenal cortex, testis, ovary, and placenta. The physiology, biochemistry, and histochemistry of ascorbic acid and vitamin D are reviewed, and recent biochemical knowledge of the thyroid, an evaluation of procedures for the cytological localization of ketosteroids, and the synthesis of cortisone and related steroids are included. One of the reviews deals with the relation of pantothenic acid to adrenal cortical function and another with the endocrine aspects of chronic human malnutrition. Each review is followed by a list of references. At the end there is a cumulative subject index covering previous volumes 6 to 10, with separate author and subject indexes for the current volume. The binding, printing, and paper are excellent. The book will be of interest chiefly to those engaged in advanced study and investigation of the metabolic relationships of vitamins and hormones.

Ciba Foundation Colloquia on Endocrinology. Volume V: Bioassay of Anterior Pituitary and Adrenocortical Hormones. General editor for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B. Assisted by Margaret P. Cameron, M.A., A.B.L.S. Cloth. $6. Pp. 228, with 53 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1953.

This symposium of 22 papers is devoted to the methodology, interpretation, and uses of bioassay procedures for hormones of the anterior pituitary gland and the adrenal cortex. The colloquium, which took place in England during March, 1952, was attended by 50 qualified workers from the United Kingdom, France, and the United States. The papers are accompanied by a stenographic report of the informal discussions that followed. The proceedings actually comprise a series of progress reports on current research work rather than a formal summary of existing knowledge in the field. The book will, therefore, be of greatest use to investigators and clinicians who are actively engaged in this specialized work.

The basic requirements for useful bioassay methods are outlined by Segaloff. Three exploratory procedures for the assay of thyrotropic hormone are presented (two involving the use of radioactive phosphorus and one in which radioactive iodine is used), but it is doubtful that the sensitivity attained is great enough for clinical use. Consideration of the complex matter of measuring gonadotropins is highlighted by an excellent discussion by Loraine on the clinical applications of some of these techniques. Of particular interest is his failure to confirm the value of pregnanediol excretion and serum chorionic gonadotropin determinations as prognostic criteria in pregnant diabetics. Astwood presents a provocative discussion on the nature of the pituitary factors responsible for luteotrophic activity as well as the various techniques available for their measurement. Li summarizes the techniques used in the assay of the growth hormone. Stack-Dunne's report on the fractionation of corticotropin reflects the existing uncertainty regarding the true character of anterior pituitary hormones. The papers of Ingle (bioassay of adrenal steroids by the muscle work test), Nelson (chemical measurement of blood corticosteroids), and Busch (paper chromatography of urinary and blood steroids) indicate the great progress that has been made in the identification and measurement of the multiple products of the adrenal cortex. Despite the technical nature of the papers the book is, in the main, eminently readable.

Lesions of the Lumbar Intervertebral Disc with Special Reference to Rupture of the Annulus Fibrosus with Herniation of the Nucleus Pulposus. By R. Glen Spurling, M.D., Clinical Professor of Surgery (Neurosurgery), University of Louisville School of Medicine, Louisville. Publication number 177, American Lecture Series, monograph in Bannerstone division of American Lectures in Surgery, edited by Michael E. De Bakey, M.D., Professor of Surgery and Chairman of Department of Surgery, Baylor University College of Medicine, Houston, Texas, and R. Glen Spurling, M.D. Neurosurgical Division editor: Barnes Woodhall, M.D., Professor of Neurosurgery, Duke Hospital, Durham, N. C. Cloth. $4.75. Pp. 148, with 45 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

This monograph is beautifully written, well illustrated, and covers the subject from embryology and anatomy to definitive treatment. Accuracy of diagnosis and conservatism in the management of patients with low back and sciatic pain are emphasized. Dr. Spurling's experience in the surgery of lumbar intervertebral disks has been extensive, and the analysis of the courses of the patients operated on by him constitutes a very impressive argument for his contention that spinal fusion in conjunction with removal of an intervertebral disk is rarely necessary. Dr. Spurling does not agree with the few neurosurgeons and many orthopedic surgeons who contend that any spine from which an intervertebral disk has been removed is very likely to be unstable and that the patient will have persistent backache as a permanent factor of partial disability unless the spine is surgically fused. Spontaneous fusion does occur in some instances in which an inflammatory process starts in the articular facets at the time of surgery. Such a spontaneous fusion, however, occurs slowly, and throughout the entire period of convalescence of six months to a year the patient may be suffering pain that could have been relieved by fusion at the time of surgery. This is a valuable book that can be used either as a textbook or as a reference book for all who are interested in injuries to the lumbosacral spine and the treatment of rupture or disintegration of the lumbar intervertebral disks.

The Winslow Weight Watcher: A Complete Course in Nutrition for Those Who Want to Lose Weight. By Thyra Samter Winslow. With foreword by Dr. Leonid Kotkin. Cloth. $3.50. Pp. 384. Abelard Press, Inc., 381 Fourth Ave., New York 16, 1953.

Every doctor who treats overweight patients will want to know about this book, because the author has so frequently requested her readers to see their doctor, to show this book to their doctor, and to ask their doctor what he thinks of the "Weight Watcher" pattern of reducing that many patients will be following her advice. The basic theory of weight reduction recommended by Miss Winslow is the intake of at least 70 gm. of protein, therapeutic doses of vitamins and minerals, and a reduction of the intake of carbohydrates and fats to the point where the total caloric intake is below that needed for the maintenance of body weight. She is extremely critical of all fads and short-term diets, because the physicians on whom she depends for advice believe that a person who tends toward obesity must be on a reduced caloric intake throughout his lifetime and that any diet lasting days or weeks is inadequate to meet this person's needs. The only way such weight maintenance can be continued indefinitely, according to Miss Winslow, is for each person to have enough understanding of the basic principles of nutrition, food, diet selection, energy needs, and other related factors to use good judgment in the qualitative and quantitative selection of his daily diet.

Miss Winslow was overweight, and she accomplished a major weight reduction under medical supervision. She became so impressed by the seriousness of the problem of obesity that she turned her writing talents to the expression of medical ideas in a very entertaining manner. Some question might be raised about her endorsement as well as criticism of named trademarked food products for those who wish to reduce, but generally her advice appears to be reasonably sound, and it is given in an emotional tone that would stimulate the obese person to at least consider reducing.

Flying Doctor Calling: The Flying Doctor Service of Australia. By Ernestine Hill. Published in conjunction with Flying Doctor Service of Australia. First American edition. Cloth. $5. Pp. 156, with illustrations. Angus & Robertson, Ltd., 89 Castlereagh St., Sydney, N.S.W., Australia; 48 Bloomsbury St., London, W.C.1, [1947]; Anglobooks, 475 Fifth Ave., New York 17, 1954.

This thrilling account of the medical service to the sparsely populated interior of Australia is written in popular style for the laity. The Reverend John Flynn, appreciating the problem, set out to do something about it. In 1912 he founded the Australian Inland Mission. In 1917 the mission board began advocating the establishment of radio communications and airborne doctors. It was not until 1928 that the first mission radio station was erected, and it did not begin operations until 1929. Two years later Allan Vickers became the first of the flying doctors. The service now has about 24 base radio stations. By means of this service instructions in the first aid treatment of patients in isolated places may be given, and if necessary, doctor and nurse are flown to the patient. Patients needing hospitalization are flown to one of the mission infirmaries. The service has saved many lives that otherwise could not have been saved. The book is illustrated with maps and photographs. There is no index.

Causality in Natural Science. By Victor F. Lenzen, Ph.D., Professor of Physics, University of California, Berkeley. Publication number 213, American Lectures Series, monograph in American Lectures in Philosophy. Edited by Marvin Farber, Ph.D. Cloth. $3. Pp. 121. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1954.

Since physicians are frequently tempted to make excursions outside of their proper field and are perhaps especially prone to undertake amateur philosophizing, it is well to be aware of the existence of books like this one. It is a laconic, well-digested review of existing ideas about causal relationships among phenomena. Much of it is condensed to such a degree that it cannot be completely understood without referring to the sources listed in the bibliography; the mathematics, as on page 93, is of a sort that baffles even a proficient student of differential and integral calculus; there is much use of ambiguous words like function, control, and operator, and in the typography used, Planck's constant "h" sometimes is in danger of going unrecognized because it looks like a "b." The book is, however, scholarly, well indexed, artistically printed, and attractively bound. It is recommended to anyone seriously interested in philosophy.

Holt Pediatrics. By L. Emmett Holt, Jr., Professor of Pediatrics, New York University College of Medicine, New York, and Rustin McIntosh, Carpentier Professor of Pediatrics, Columbia University, New York. Twelfth edition [of "Diseases of Infancy and Childhood"]. Cloth. $15. Pp. 1485, with 271 illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1953.

This all-inclusive textbook in pediatrics has been edited by the present authors since 1926. There are 72 well-qualified contributors. With the rapid advances in the various fields of medicine, it is difficult to keep a standard text of this type up-to-date. It would be advantageous for such a book as this to be in loose-leaf form, so that new information can be added as some of the old becomes outdated. The book is exceptionally well written and would be an excellent addition to the library of the medical student and the pediatrician.

Clinical Orthopaedics. Number 2. Editor-in-Chief: Anthony F. DePalma, with assistance of five associate editors and board of six advisory editors. Cloth. $6. Pp. 247, with 232 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1953.

This is the second volume of a series of correlated monographs on subjects of special interest to orthopedists and all who have to do with bone and joint lesions. Section 1 deals with intramedullary nailing of fractures. The indications, technique, complications, and results of this method of treatment are described in detail by qualified surgeons. Excellent prints of roentgenograms illustrate the text. Comprehensive bibliographies supplement each paper. Each subject is dealt with in clear and concise manner. Section 2 contains papers on gross osteopathology of arthritis, ischial apophysiolysis, Phemister's bone graft of the tibia, osteoid osteoma, fusion of the ankle joint, congenital metatarsus varus, Durham flatfoot plasty, tuberculosis of the hip, and giant-cell tumor of the radius. These authoritative papers are profusely illustrated. The format is pleasing, and a complete index is appended. Surgeons dealing with fractures and other bone lesions should profit from a perusal of this volume.

Maladies médicamenteuses d'ordre thérapeutique et accidentel. Par Claude Albahary. Avec le concours de D. Christol, et al. Préface de A. Tzanck. Cloth. 5000 francs. Pp. 752, with 55 illustrations. Masson & Cie, 120 boulevard Saint-Germain, Paris, 6e, 1953.

The availability to the modern physician of a host of potent drugs requires his acquaintance not only with their therapeutic virtues but also with their toxic potentialities. Useful drugs that normally are relatively innocuous may, under certain circumstances in susceptible persons, induce effects that may prove fatal. These toxic effects are often unnoticed in the presence of the underlying disease unless the physician is acquainted with their nature and alert to their appearance.

This volume is an excellent and thorough review of the toxic effects of all drugs in common use. After a brief résumé of the normal action and uses of each drug, the author describes their toxicology when used as therapeutic agents as well as when misused or taken with suicidal intent. This description is followed by a detailed discussion of available methods of treatment for the adverse effects of the drugs. The information included is thorough, sound, and up-to-date; there are ample references to the original literature. The book is clearly written, well arranged, and well printed. The illustrations are well chosen and are original. This book may be read with profit by every physician in order that he be aware of the toxic potentialities of the potent medicaments at his disposal and acquainted with the procedure for treating the adverse effects that are at times inevitable.

Fundamentals of Biochemistry in Clinical Medicine. By Niels C. Klendshoj, M.D., Assistant Professor of Pathology, University of Buffalo, School of Medicine, Buffalo, New York. Cloth. $7.75. Pp. 276, with 9 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

The book opens with two chapters on atomic and molecular structure, which are out of place in a book of this nature. The next seven chapters give brief reviews of acid-base relations, body fluids, enzymes, lipids, proteins, carbohydrates, and porphyrins. The remainder of the book is devoted to the practical phases of clinical biochemistry under the following topics: the liver and the biliary tract, the kidneys and the urinary tract, the hypophysis, the thyroid, the pancreas, the adrenal glands, disorders of the bones, the nervous system, and nutrition. The preface states that the book is designed for the reader whose main interest is not in this field and that the book is to serve as a brief review on matters of clinical biochemistry. It is not intended as a reference work, and as such the value of the book to the physician would be limited to its use as a refresher outline if he has lost contact with the general principles of clinical biochemistry.

Dizziness: An Evaluation and Classification. By David Downs DeWeese, M.D., Clinical Professor of Otolaryngology, University of Oregon Medical School, Portland, Oregon. Publication number 176, American Lecture Series, monograph in American Lectures in Internal Medicine. Edited by Roscoe L. Pullen, M.D., F.A.C.P., Professor of Medicine and Dean, University of Missouri School of Medicine, Columbia, Missouri. Cloth. $2.75. Pp. 80, with 2 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1954.

In this concise monograph, the author evaluates the common symptom of dizziness and classifies its possible etiological factors so as to establish a basis for rational therapy. Since dizziness is produced by a wide variety of conditions, physicians are urged to maintain an attitude of awareness to disease in all parts of the body. Close attention to the history and to clinical details will often make differential diagnosis easier. For physicians with a limited amount of reading time, this small book will be suitable for a quick review of the subject.

QUERIES AND MINOR NOTES

NEW TEST FOR HYDROCHLORIC ACID IN STOMACH

TO THE EDITOR:—*Please describe the new method in which Diagnex is used to determine gastric hydrochloric acid.*

Melvin B. Lamberth Jr., M.D., Kilmarnock, Va.

ANSWER.—The quinine carbacrylic resin (Diagnex) test determines the presence of free hydrochloric acid in the stomach without the necessity of intubation. The procedure is as follows: 1. A capsule containing 250 mg. of caffeine sodium benzoate acts as a stimulant of gastric secretions. After the first morning urine is discarded and with no breakfast being eaten, the contents of this capsule are taken with water or plain tea or coffee. A control urine specimen is obtained in one hour. 2. Two grams of quinine carbacrylic resin granules are taken in one-fourth glass of water, followed by another one-fourth glass of water. A newer simplified technique consists of obtaining one urine specimen two hours after taking the granules. Each of the urine specimens is diluted with distilled water to 300 cc. To 30 cc. of this solution is added 0.5 cc. of half-normal sodium hydroxide followed by extraction with 15 cc. of ether. Next, 8.2 cc. of the ether layer is placed in a test tube and to this is added 5 cc. of tenth-normal sulfuric acid. If quinine is present, the solution will have a fluorescence that is detected with the aid of a photoelectric fluorophotometer or some other method of comparison with standard quinine solutions. These are made with either Diagnex standard tablets (containing quinine hydrochloride) or quinine sulfate solution (the fluorescence may be interfered with by concomitant treatment of the patient with quinine, vitamin B complex, or steroid compounds).

In the absence of hydrochloric acid in the gastric contents, the quininium resin passes through the gastrointestinal tract unchanged. In the presence of hydrochloric acid, quinine is displaced by the hydrogen ions of the acid and absorbed; 15 to 20% of the disassociated quinine is excreted in the urine within two hours. If the equivalent of 25 mcg. or more of quinine is present in the two hour urine sample, the result is considered positive and free hydrochloric acid is present. However, if there is a 15 to 25 mcg. equivalent, the test should be repeated in five to seven days. Recovery of less than 15 mcg. constitutes a negative result.

The quinine carbacrylic resin test is a qualitative, but not a quantitative, indication of the presence of hydrochloric acid in the gastric contents. It is particularly useful for screening and for patients who are distressed by passage of a tube for gastric aspiration or in whom there is a contraindication to the passage. However, a positive result is not quantitative, and if there is a negative result (indicating no free hydrochloric acid), the test should be repeated. A negative result is an indication for intubation of the stomach following an Ewald meal. If free hydrochloric acid is absent, 0.3 mg. of histamine should be given hypodermically, followed by gastric aspiration in 30 minutes. The quinine carbacrylic resin test is recommended as a useful method of selecting patients who require further study.

SULFONAMIDES AND X-RAYS

TO THE EDITOR:—*Please inform me about untoward reactions that have occurred when sulfonamide therapy and x-ray therapy have been given at the same time?*

Robert P. Meader, M.D., Butler, Pa.

ANSWER.—While the phenomenon of photosensitization is well known as a factor in the production of rashes in patients who are receiving sulfonamide therapy, there is little or no controlled evidence that toxic reactions may arise from the use of roentgen therapy in patients who are receiving sulfonamides. By this it is meant that evidence appears to be lacking that roentgen therapy and sulfonamides have either an additive or a synergistic effect in producing damage to the hematopoietic system.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

AMERICAN HEART ASSOCIATION

TO THE EDITOR:—*Please tell me how patients with heart disease can receive help from the American Heart Association, A woman about 35 with three children has valvular damage from rheumatic heart disease. Her husband is no longer able to pay for her hospitalization, and she is not getting proper care at home.* *Lois C. Wyatt, M.D., Kirkwood, Mo.*

ANSWER.—One of the three major programs of the American Heart Association is that of community services (the other two being the support of research and the program of professional and lay education). However, because of the overwhelming number of persons in the United States who suffer from heart disease and who may be in need of direct financial or other care, it is the policy of the association not to provide individual patient care, such as the payment of medical fees or hospital bills, private and nursing home care, or the furnishing of drugs. Such services or the financing of them should be sought locally from other agencies, such as welfare agencies, benevolent societies, and community welfare funds, and through the good offices of the medical profession.

Benefits offered by the American Heart Association or by its affiliated and local heart associations to the individual in the local community are ordinarily presented in the form of such group and community services as the establishment and maintenance of cardiac clinics, the development of programs of public information and education, and the establishment of professional education programs aimed at the local physicians. In some areas where the local heart association is sufficiently developed, cardiac children's camps, rehabilitation centers, and other facilities are supported in part or as a whole. In instances of individual need, the local heart association should be consulted for advice on the particular problem presented. When the local association is unable to provide a solution, its staff will consult with other agencies or with the local medical profession in an effort to discover a source of assistance.

ELDERLY PRIMIGRAVIDA

TO THE EDITOR:—*A 32-year-old woman is contemplating marriage to a man of 35. This is the first marriage for both. He will not permit her to have a baby, as it will endanger her life. She wants a baby. Both are well and healthy. With present day technique, is it considered dangerous for a woman of 32 to have her first baby?*

M.D., Pennsylvania.

ANSWER.—Greenhill (Principles and Practice of Obstetrics; ed. 10, Philadelphia, W. B. Saunders Company, 1951, p. 632) says, "The best years for women to bear children are from 20 to 25. After 35 the function is attended with increasing difficulties, although these are exaggerated by most physicians and patients. It is considered that a woman giving birth to her first baby after she is 35 years of age is an elderly or old primigravida. Such women are more likely to have hypertension, toxemia, disturbances in labor, fibromyomas, adenomas of the thyroid and carcinoma of the cervix than are women less than 35 years of age. At the Mayo Clinic, according to Randall and Taylor, preexisting hypertension was present in only 1% of all pregnant women, whereas the incidence before pregnancy or very early in gestation in women more than 35 years was 11.6%. . . . The mortality was more than three times as high for the babies of women 35 years or older than

in those less than 30 (9.2 versus 2.8%). A less gloomy picture is reported by Waters and Wager who maintain that their figures do not establish elderly primigravidity as a grave maternal life threat, whether the delivery is normal or operative. The risk is obviously greater but the differential between old and young primigravidas is certainly not remarkable. They maintain that pregnancy after the age of 35 may be contemplated with reason, approached with intelligence and confidence and managed before, during and after parturition with complete awareness of the potential hazards. However, adequate preparations for threatened complications and conservative intervention should be made. . . . I fully agree that if a woman places herself in the hands of an experienced obstetrician, age alone should not deter her from becoming pregnant. The oldest primigravida I have delivered was 49 and the oldest multigravida was 52. With neither one was there any trouble in pregnancy or labor. Primigravidity in advanced years should be a factor influencing the indications for cesarean section. Advanced age in itself should not be an indication for abdominal delivery but when it is associated with some factor that is a borderline indication for operative intervention, such as a moderately contracted pelvis, breech presentation or preeclamptic toxemia, the operation is justified. In old primigravidas more importance should be attached to the baby than in younger women."

Eastman (Williams Obstetrics, ed. 10, New York, Appleton-Century-Crofts, Inc., 1950, p. 1101) says, "When a woman has her first pregnancy at the age of 35 or beyond she is called an 'elderly primigravida.' . . . Certain complications inimical to the successful childbearing are observed with greater frequency in this group of patients; notably chronic hypertensive vascular disease, myomata, uterine inertia and failure of the fetal head to engage at the onset of labor. As a consequence, the outlook for the baby is somewhat less favorable in elderly primigravidas. . . . Cesarean section is indicated more often than usual. It was performed in 26.7% of such cases at the Johns Hopkins Hospital. It must not be deduced however from what has been said that cesarean section is always indicated in elderly primigravidae or even in the majority of the cases. But when such a patient presents a substantial complication, cesarean section is indicated more often than is the case with younger women presenting the same complication."

CHRONIC GINGIVITIS

To the Editor:—*What would cause gingivitis that has affected a woman for many years? The condition is confined to the labial side of the gums. Partial healing takes place in a matter of days, only to break down within 24 hours. Incomplete healing is preceded by peeling of the outer layer of the mucosa. The gums are spongy around the teeth. Nothing abnormal was revealed by hematological and serologic tests. No benefit came from ingestion of different vitamins singly or in combination. Several dental surgeons treated this woman over a long time without benefit. A smear examined for "trench mouth" infection was reported negative. Urinalysis does not reveal albumin and sugar. Use of many local antiseptics and mouth washes, including penicillin troches, gave no results.* *M.D., California.*

Answer.—There are several questions that should be answered before a diagnosis can be made. Does the patient wear any dentures? Has she both gold and amalgam fillings in her teeth? Frequently the oral mucosa is sensitive to the compounds used in construction of a denture. Also often a chemical or electrical reaction between two different metals is responsible for a deposit on the gums. It should also be determined whether the patient has been in the habit of chewing gum or sucking on lozenges. Since it is assumed that ulceromembranous gingivitis (trench mouth) and constitutional disorders have been excluded, it appears most likely that the condition is due to local irritation or hypersensitivity. It is suggested that an analysis of the foreign materials in the mouth be made and that cultures be made from the exudate for bacterial analysis for both aerobic and anaerobic organisms. Antibiotics in the form of lozenges should be banned. The lesions should be touched with silver nitrate solution followed by the application of gentian violet. Gentian violet application should be continued even after the exudate has disappeared.

PINWORMS

To the Editor:—*I have treated a resistant case of pinworm infestation in a family of three (mother, father, and daughter) with p-benzylphenylcarbamate (Diphenan) wafers, gentian violet capsules, and oxytetracycline (Terramycin) (5 gm.) with the usual purgatives, enemas, and thorough house cleaning, including boiling of clothing and bed clothes. The family even moved to a new house, but still the infection persists. The mother and daughter have severe cases of pruritus ani. I would like some further suggestions as to treatment and care.*

Alexander D. Kovacs, M.D., Plainfield, N. J.

Answer.—Recently Brown and associates (*New York Acad. Sc.* **55**:6 [Dec. 30] 1952) demonstrated that oxytetracycline (Terramycin) is as effective as gentian violet for eradicating pinworms, with a cure rate approaching 100% if all infected persons take the full course. The scheduled dosage is as follows: For children from 2 to 5 the dosage is 100 mg. four times daily for two days, then 50 mg. four times daily for two days, and finally 50 mg. daily for 14 days. For children from 6 to 10 the dosage is 250 mg. four times daily for two days, then 250 mg. two times daily for two days, and finally 250 mg. daily for 14 days. For children over 11 and adults the dosage is 500 mg. four times daily for two days, then 250 mg. four times daily for two days, and finally 250 mg. daily for 14 days. For small children unable to swallow capsules, powdered oxytetracycline may be spread on bread.

SMALL GALLBLADDER IN YOUNG GIRL

To the Editor:—*A 6-year-old girl has a gallbladder the size of a small peanut, and it does not empty with a fatty meal. I have never seen one this small and would appreciate your comment.* *Louis L. Sherman, M.D., Oakland, Calif.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—A rudimentary gallbladder in a 6-year-old girl is undoubtedly the result of a congenital abnormality. This sometimes manifests itself in a complete absence or partial absence of the extrahepatic biliary ducts and accessory structures. In this patient it is quite probable that a compensatory dilatation of the common bile duct will take place and that no abnormalities in digestive and absorptive functions dependent on bile in the intestinal tract will result. There are insufficient data to determine whether such a rudimentary gallbladder is more or less susceptible to stone formation than a gallbladder of normal size.

Answer.—There is probably no clinical significance in the fact that a 6-year-old girl has a gallbladder shadow that is the size of a small peanut and that does not empty with a fatty meal. The gallbladder test should be repeated later if there is a clinical indication.

"INJECTIONS" WEEKLY FOR THIRTY YEARS

To the Editor:—*What should constitute future treatment of a 73-year-old woman who states she was told she had syphilis 40 years ago and has been given "injections" once or twice weekly (penicillin during the past 2 or 3 years) for 30 years! Her Kahn-Kline reaction at present is "strongly positive 4 units." She has no subjective symptoms.*

M.D., Indiana.

Answer.—Let her alone. A woman of 73 with no symptoms of syphilis and presumably no physical signs (not stated) who has been as fantastically overtreated as has this patient should be told to forget the whole business. Syphilis is certainly a matter of no moment to her health. Her persistently positive blood test may be disregarded.

GOITER IN AN INFANT

To the Editor:—*A friend had a goiter operation. She did not know what type. Later she had a baby with a lump in the neck that was called a goiter. Is that rare? What treatment is necessary in such a case?* *M.D., Kansas.*

Answer.—There is a tendency for thyroid dyscrasias to run in families. For instance, in a series of 18 children with thyrotoxicosis seen in this clinic recently, 50% had a family history of thyroid disease. Infants have a goiter during the neonatal period for one of several reasons: (*a*) severe maternal iodine lack, (*b*) intensive iodide therapy to the mother, (*c*) thiouracil therapy to the mother, and (*d*) idiopathic congenital thyroid disorders. The first (*a*) and last (*d*) types are apt to be characterized by a tendency to infantile hypothyroidism. When this is so, thyroid hormone substitution therapy is indicated. Infants with the second type (*b*) may appear thyrotoxic for a few weeks. Except for a rarely indicated isthmectomy for relief of mechanical obstruction to the trachea and great vessels, these patients need no therapy. Patients with the third type (*c*) usually require no therapy unless the goiter persists and signs of thyroid insufficiency develop. In all cases appraisal of the thyroid status by measurement of the serum butanol-extractable iodine or serum precipitable iodine is recommended.

FALSE LABOR PAINS

To the Editor:—*A woman, aged 32, para 5, gravida 6, had false labor pains at the seventh month with her fifth pregnancy and they began at the fourth month in the sixth pregnancy. They persisted until the time of termination of the fifth pregnancy and have been constant since the fourth month during this pregnancy. Please discuss the cause and remedy.* *Walter A. Porter, M.D., Hillsville, Va.*

Answer.—False labor pains normally begin during the last three or four weeks before the onset of labor. They are merely an exaggeration of the intermittent uterine contractions that occur throughout pregnancy but are rarely associated with discomfort. False pains differ from labor contractions in that they have no pattern. They come at irregular intervals and last varying periods. When they have their onset in late pregnancy they do result in progressive cervical effacement. Why false labor pains occur in midpregnancy is not known. No specific therapy is indicated, but rest and barbiturates may help.

LIPEMIA AND WORK IN A DOUGHNUT SHOP

To the Editor:—*A 46-year-old man had a fairly severe posterior coronary occlusion. His progress has been satisfactory. Although he is slender, I suggested that he restrict ingestion of fats, and at this suggestion this information was brought forth. He works in a doughnut shop and stands over vats of hot grease. Apparently everything in the region becomes penetrated by grease. When he last donated blood for the Red Cross, the nurse stated there was fat in his blood. Could it be that he absorbs this fat from the lungs in sufficient amount to be harmful?* *John W. Bradshaw, M.D., Ashland, Ore.*

Answer.—The scientific literature contains no references, as far as could be ascertained, to lipemia resulting from pulmonary absorption of neutral fats. The effect produced by inhalation of lipids is rather an intense pulmonary inflammatory reaction, with lipid pneumonia. In a man, aged 46, with a history of a recent myocardial infarction, the routine observation of grossly lipemic plasma or serum (assuming the patient was in the postabsorptive state) should lead the physician to suspect endogenous hyperlipemia, probably of the hypercholesterolemia (xanthomatotic) type. Serum analysis should be done for total lipid, cholesterol, phospholipid, fatty acids, and possibly lipoproteins. The presence of hypercholesterolemic hyperlipemia would indicate an endogenous xanthomatotic tendency, probably familial. No evidence exists suggesting that this condition is attributable to occupational exposure to hot liquid lipid and its vapors; the definitive proof would of course be to remove the patient from his work environment for a period and determine the effect (if any) on the lipemia.

SMOG IN SOUTHERN CALIFORNIA

To the Editor:—*Friends of mine visiting in Southern California have complained that the smog caused dryness of the throat and watering of the eyes. Is there any therapy that might help in this condition?*

Milton E. Bork, M.D., Buffalo, N. Y.

Answer.—In reply to the smog question, in Los Angeles the only symptoms encountered are watering of the eyes and a dryness of the pharynx plus a little cough. Examination shows slight conjunctivitis but no evident abnormality in the nose, pharynx, or larynx. Over the years repeated examination has not shown appreciable deleterious effects on the nasal, pharyngeal, or laryngeal mucosa. Allergic persons seem to be more susceptible to the effects of smog. No therapy is of value except local application of mild agents such as boric acid solution to the eyes and tincture of nitromersol (Metaphen) to the pharynx.

DEAFNESS FOLLOWING USE OF DIHYDROSTREPTOMYCIN

To the Editor:—*What is the prognosis of tinnitus aurum and deafness of one year's duration caused by heavy and prolonged dosage of dihydrostreptomycin with loss of half of the auditive acuity in a man 40 years old?*

M.D., South America.

Answer.—The prognosis for recovery from deafness in this case is poor. In cases in which the therapy with dihydrostreptomycin has been prolonged and the doses large, vestibular and cochlear damage does occur, although to a lesser degree than with streptomycin alone. Recent work by H. Corwin Hinshaw has shown that doses of one-half streptomycin combined with one-half dihydrostreptomycin almost never cause eighth nerve damage. It is suggested that this plan of treatment should be followed if more treatment is necessary. Some relationship has been shown as to the increased incidence of eighth nerve damage if kidney function is poor. The dosage of the combined drugs should be kept at a minimum consistent with the state of kidney function and the severity of the condition being treated.

NIGHT DREAMS

To the Editor:—*What measures would reduce night dreams?*

Jacob M. Cohan, M.D., Philadelphia.

Answer:—Night dreams are normal. Dreaming may be considered a physiological safety valve and a natural process of recuperation for the psyche just as rest and relaxation serve the physical constitution. A function of dreams is to partially relieve psychological frustrations and tensions by means of camouflaged symbolic wish-fulfillment fantasy and to help the ego to integrate these problems so as to be able to better carry out its realistic functions. If dreaming becomes so excessive as to interfere with adequate sleep, however, it may be symptomatic of an anxiety neurosis or a psychoneurosis. The mental state should then be investigated, and, if he continues unrelieved, psychiatric consultation is indicated.

TESTS FOR PHEOCHROMOCYTOMA

To the Editor:—*What are the safest and most reliable pharmacological screening tests for pheochromocytoma in hypertensive patients for use by the general practitioner?*

M.D., West Virginia.

Answer.—The safest test for pheochromocytoma is the use of phentolamine (Regitine) when the arterial pressure is elevated. The histamine test is especially useful when the pressure is low and the secretion of epinephrine and arterenol by the tumor is to be stimulated. There is relatively little danger in the use of this test, especially since the rise in blood pressure, if it becomes excessive, may be blocked by phentolamine. Piperoxan is useful but may have some very unpleasant side-effects.

TRICHOMONAS VAGINALIS

To the Editor:—*In the answer to a question on Trichomonas vaginalis infection in* The Journal, *Jan. 23, page 375, the statement is made that bladder infection will be cured if the vaginal infection is cured. There is evidence that some of the chronic or persistent vaginal trichomoniasis is due to associated inflammatory conditions of the urethra and/or bladder. These urinary lesions are determined by urethroscopic and cystoscopic examinations. Even a minor involvement may be a significant factor. Urologic treatment of these sites may be necessary and important concurrently with vaginal therapy. In some instances local hyperpyrexia to the vagina may help to eradicate the urethral and vaginal inflammation.*

The essential therapy of the vagina is to establish a normal bacterial flora. In the postmenopausal patient this can be done readily by the use of appropriate doses of estrogens. During the menacmic period it can better be accomplished by the use of lactose (alpha or beta). Other products such as gelatin may give the same result. Normally the other sugars should be avoided because these are fermented by Candida albicans whereas lactose is not. The use of the antibiotics in the vagina may reduce some of the organisms and thus may possibly enhance an exacerbation of a mycosis by a biological imbalance. For this reason antibiotics should be used topically only on definite indications until more is known of this microbiological picture. It is known that a large number of both men and women carry various bacteria, protozoa, and fungi in the intestinal tract. It is understandable why the attempted eradication of one type of organism from the intestinal tract is still a controversial point. In the chronic persistent trichomoniasis, attempted eradication by "specific" therapies may not be nearly as efficacious as the cure of mycosis. Thus the establishment of a natural vaginal bacterial flora and a normal healthy vaginal mucosa becomes more significant. The normal mucosa favors the growth of the acidophilous organisms, which by competition reduce the number of other bacteria and the Trichomonas organisms.

H. Close Hesseltine, M.D.
University of Chicago, Chicago 37.

To the Editor:—*The query on Trichomonas vaginalis in* The Journal, *Jan. 23, page 375, was interesting. In my experience, there are a few patients who harbor a primary urethral trichomoniasis focus. If the urethra is treated locally in these patients, clinical response and clearing of the trichomoniasis may ensue. I believe Dr. Dabney's patient should have careful urological examination and eradication of any chronic foci that may be found.*

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ABSENCE OF SECONDARY SEX CHARACTERISTICS

To the Editor:—*Regarding the question on absence of secondary sex characteristics in Queries and Minor Notes, Jan. 23, 1954, a few procedures may aid in differential diagnosis. Gonadotropic determinations are not available in general practice, and waiting for years to determine agenesis might lead to loss of time if specific therapy is indicated. The physical signs are specific. The bone age is probably retarded, and the basal metabolic rate is probably low. Vaginal smears at regular intervals will delineate the absence or presence of follicular activity by alterations in the desquamated cells of the vaginal epithelium. There may be evidence of some cornification, which, in the young, may be present before obvious development of secondary sexual characteristics. If present, cyclic administration of pregnant mare serum hormone or the follicle-stimulating hormone of the anterior lobe of the pituitary for two weeks every four weeks will produce objective improvement in growth, sexual characteristics, and somatic development. These results will not appear spontaneously but will progress at a rate comparable to that in normally developing prepubertal females. Vaginal smears observed during the treatment and at intervals will corroborate physical signs of ovarian stimulation.*

The efficiency of the follicle-stimulating hormones has been demonstrated by many; vaginal smears in the evaluation of ovarian development and activity has been described in the American Journal of Obstetrics and Gynecology *(6:1306 [Dec.] 1950). The administration of estrogenic hormones before the potentialities of the intrinsic ovaries are determined will only mask a possible intrinsic supply and possible therapeutic progress but cannot in any way produce stimulation of retarded ovarian development.*

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BLOOD TRANSFUSION

To the Editor:—*In* The Journal, *Aug. 15, 1953, page 1585, in the answer to a query on blood transfusion, your consultant stated: "There is no major objection to administering blood from persons of one race to those of another. . . ." While agreeing with the general statement, I wish to point out the necessity for additional tests in Negro donors (whether blood is given to same or another race). Since according to the latest census there are about 15 million Negroes in the United States, there are over a million with a sickling trait. Sicklemic blood must not be administered, since there is no benefit to the recipient. When the donor is a Negro, the following test must always be performed, as first was recommended by Scriver and Waugh and practiced by Emmel. 1. A rubber band is placed around any finger for three to five minutes to produce anoxemia (an ear lobe must never be used). 2. Two or three drops of blood on a slide are covered by a cover slip and surrounded by a rim of white petrolatum (Vaseline) to exclude oxygen. 3. The blood is observed under a microscope every 30 minutes, if time permits, for about 24 hours. Sickling cells may appear from within a few minutes to a few hours. This procedure is important for Negroes themselves, as giving sicklemic blood not only will not benefit the patient but will deprive the donor of oxygen-carrying cells badly needed in his circulation.*

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FREQUENT DESIRE TO URINATE

To the Editor:—*In* The Journal, *Aug. 15, 1953, page 1586, was a query on "Frequent Desire to Urinate." The request for information on a 72-year-old woman with Parkinson's disease does not seem to be answered correctly. I doubt if urinary calculi would be the commonest condition found, and the consultant did not stress the importance of an adequate urethroscopic examination. If such an examination were made, I feel reasonably sure that residual urine, probably infected, would be found in this patient and perhaps a bladder neck contracture. The bladder probably would be trabeculated. If these conditions exist, and they certainly are more likely than calculi (unless they are secondary), then she should have the advantage of transurethral bladder neck resection. Such a procedure in a male will give good results, though admittedly not as good in a case of Parkinson's disease as in ordinary prostatism. A man or woman with or without Parkinson's disease should have an adequate urinary survey including x-ray study for the symptoms described by the inquiring physician. I think drugs should be used as a last resort, as surgical correction of the anatomical and pathological causes would be more logical.*

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